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LUDWIG'S ANGINA

AN ANALYSIS OF FORTY-FIVE CASES

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WILHELM FRIEDRICH VON LUDWIG,[4, 15] in 1836, published a report of the disease which now bears his name. A large number of communications on the subject have since appeared in the literature of all languages. Some of these communications have dealt with the etiologic bacterial agents involved. Others have attempted to disclose the exact pathogenesis and spread of the infection. Most have referred to the importance of having an exact knowledge of the anatomic structures in the neck and the floor of the mouth. All, however, have agreed that the disease is very serious and often fatal. The cause for the mortality has been attributed largely to some peculiar and cryptic virulence of the infecting organisms which rapidly overwhelms the patient and leads to his death, often a very sudden one. In 1908, in a detailed and admirable discussion of the subject, Thomas[21] pointed out that the majority of the deaths were due not to sepsis but rather to a mechanical respiratory obstruction. He related this obstruction directly to the narrow and unyielding boundaries within which the infection is tensely confined. He advised early operation for the relief of tension in the involved space, and recommended that the operation be performed under local anesthesia. The mortality rate in many series[1, 2, 8, 21, 22, 23, 25] has continued, nevertheless, to lie between the high brackets of 25 and 54 per cent.

It is not our purpose to enter here into involved and scholastic disputations relating to the exact points of origin of the infection, its spread by fascial spaces or lymphatics, or its primary or secondary nature. We do not mean to minimize the importance of these considerations in the study of the disease, but they do not happen to concern our present primary purpose. We wish, rather, to devote ourselves to the

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task of dispelling the myth, still prevalent in many quarters, that Ludwig's angina is a sinister affliction endowed with some sort of mysterious and unalterably fatal sting. We wish to emphasize that when the disease is recognized early and is treated promptly and judiciously, the mortality rate will drop precipitantly. We shall support our contentions by an analysis of the cases treated at the New Haven Hospital over a period of twenty years.

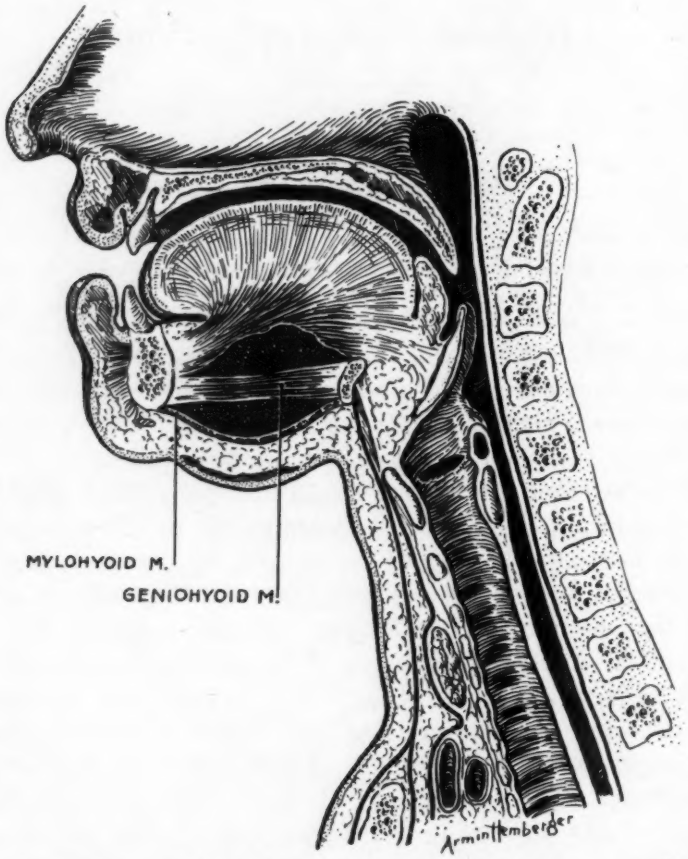

Fig. 1.—Diagrammatic sketch showing the location of pus in the submandibular space. (From Christopher, Frederick: *A Textbook of Surgery*, W. B. Saunders Company.)

CRITERIA FOR MAKING THE DIAGNOSIS

There has been a good deal of discussion as to what really constitutes Ludwig's angina. The term has often been loosely applied to any infection in the upper part of the neck, especially when it is associated with a brawny nonsuppurative induration and when it appears to be of a violent nature. We have included in our series only those infectious processes located in the areas between the mylohyoid and the geniohyoid, or between the geniohyoid and the genioglossus muscles (Figs. 1 and 2) regardless of the etiology, the point of origin, or the pathway of spread

of that infection. The anatomic structures limiting these areas, the so-called submandibular space,[10, 11, 12] have been adequately described by others.[1, 3, 6, 10, 11, 12, 21, 23] No attempt will be made, therefore, to repeat these descriptions. An infectious process, whether associated with suppuration or with edema alone, will increase the tension within this space and will displace the only yielding bordering structures, namely, the floor of the mouth, the tongue, and the pharynx. It is this displacement which is in a large measure responsible for the respiratory difficulties so characteristic of the disease. The edematous tongue is often

Fig. 2.—Diagrammatic sketch showing the diaphragm formed by the structures in the floor of the mouth. (From Christopher, Frederick: *A Textbook of Surgery*, W. B. Saunders Company.)

elevated to such an extent that the oral and pharyngeal cavities are almost completely filled. The displaced pharynx carries the epiglottis and larynx with it, and thus there is further encroachment upon an already seriously compromised airway. Because of its close proximity to the site of infection and because also of adjacent venous obstruction, the larynx itself may suddenly be involved in a rapidly progressive edema and become completely obstructed. Since the infection lies deep to the mylohyoid muscle and the cervical fascia, the skin of the neck in the submandibular and submaxillary areas will not be involved early in the disease and will slide freely over the underlying swollen and indurated tissues. Similarly, fluctuation is not an early sign and is almost invariably absent in the initial stages of the illness. Often no pus is present and the local distortion of the tissues is caused only by edema

associated with the cellulitis. However, even when present, the pus is so deep and so tensely confined that the characteristic sign of fluctuation cannot be elicited. The earliest and therefore the most important clinical manifestations of an infection within the submandibular space, and the ones which we have used as criteria for making the diagnosis of Ludwig's angina are: (1) a deep and tender swelling in the submaxillary and submandibular areas of the neck; (2) swelling of the floor of the mouth; (3) elevation of the tongue. The systemic manifestations are generally the same as those in any other infectious process of similar nature and extent. The clinical diagnosis was verified by operation in forty-three of our cases, and in the remaining two by a spontaneous rupture of the abscess through the mucous membrane of the floor of the mouth. Dysphagia, hoarseness, dyspnea, pneumonia, and septicemia are all later arrivals, and one should not wait for them before recognizing the true nature of the disease.

ANALYSIS OF CASES

Forty-five patients were treated for Ludwig's angina at the New Haven Hospital between the years 1922 and 1941 inclusive. There were thirty males and fifteen females. The ages varied from 5 to 67 years. There were two in the first decade of life, eleven in the second, twelve in the third, six in the fourth, eight in the fifth, two in the sixth and four in the seventh.

Antecedent Factors.—Infected teeth were responsible for the onset of the disease in thirty-one cases. In nineteen there was a history of a recent lower molar tooth extraction. Twelve patients had complained of lower molar toothache. Apical abscesses were subsequently revealed in some of these by x-ray examination. There were two instances of trauma to the floor of the mouth by foreign bodies, glass in one and a wisp of hay in the other. Two patients had had a previous submaxillary adenitis, two had compound fractures of the mandible, four had "sore throats," and one had lupus erythematosus with multiple mucous membrane lesions. In three cases nc antecedent cause of any kind could be discovered.

Duration of Symptoms Before Admission to the Hospital.—This period varied from 18 hours to seven days, the average being about three days.

Signs and Symptoms.—All the patients were ill and presented themselves on admission with sharp and significant rises in temperature, pulse, and blood leucocyte count. All complained of a painful swelling in the submaxillary and submandibular areas of the neck. Swelling of the floor of the mouth and elevation of the tongue were present in forty-four cases. The remaining patient had such severe trismus that the mouth could not be opened sufficiently for adequate examination. Dysphagia was recorded in forty-one instances. Thirteen of the patients

complained of dyspnea. Some of the others who did not have dyspnea were hoarse. Trismus was present in more than one-half of the instances where it had been specifically mentioned.

Interval Between Admission to Hospital and Operation.—Thirty-two patients were operated upon immediately after admission, six on the first day, five on the second day, and three on the fourth day.

Operation.—Forty-six operations were performed in forty-three patients. The surgeons included many different members of the house and attending staffs. In three of the patients there was a subsequent spread of a unilateral infection to the opposite side which required, in each instance, a second operation. The remaining forty were each operated upon once. In two patients the infection subsided without operation, after spontaneous rupture of an abscess through the floor of the mouth.

Anesthesia.—Local novocain infiltration anesthesia was employed in forty-two operations. General inhalation anesthesia was used four times, once in a child five years old, once in a child seven years old, and twice in the same adult.

Operative Findings.—Frank pus (few drops to many cubic centimeters) was drained in thirty-five of the operations. Edema alone but no pus was found in eleven instances.

Bacteriologic Fndings.—The majority of the cultures revealed the presence of more than one organism in the pus. The combinations were multiple and varied. The organisms were of the usual variety commonly found in any series of ordinary abscesses and included hemolytic streptococcus, nonhemolytic streptococcus, *Streptococcus viridans, Staphylococcus aureus, Staphylococcus albus,* spirochaetes and fusiform bacilli, *Haemophilus influenzae, Bacillus coli,* and diphtheroids. In the group where only edema was present the wound culture was sterile in four instances, *Staph. aureus* was cultured in two, *Staph. albus* in one, and spirochaetes and fusiform bacilli in one. In the remaining three cases the results of the cultures were not recorded.

Course After Operation.—In the survivals there was an immediate relief of symptoms following the operative procedure. The edema of the floor of the mouth and the elevation of the tongue rapidly subsided. The temperature and pulse fell to normal limits after about seven days. The wounds healed after draining for a period of several weeks.

Mortality.—There were two deaths. Autopsies were performed in both fatal cases. One had a dissecting aortic aneurysm which had suddenly ruptured into the thorax. The other had a concomitant suppurative cavernous sinus thrombophlebitis, lung abscess, and pneumonia.

Tracheotomy.—Tracheotomy was performed three times: in one patient as an emergency procedure immediately after admission to the hospital and while en route to the operating room; in the second patient, six hours after an inadequate operation had been performed; in the third patient, twelve hours after an adequate operation.

Complications.—Pneumonia, lung abscess, and cavernous sinus thrombophlebitis were present once. All occurred in the same patient. It is probable that the pneumonia and lung abscess were complications of the cavernous sinus thrombophlebitis rather than of the Ludwig's angina. It is probable also that the cavernous sinus thrombophlebitis was a coeval infection and did not originate from the angina. There were no instances of mediastinitis.

SUMMARY AND DISCUSSION

Ludwig's angina is a disease which is attended with a constant threat to the life line of the upper air passages and which therefore demands immediate emergency treatment. Fortunately, there are distinctive clinical manifestations which appear very early in the disease and can be easily recognized. The local diagnostic criteria are an external tender swelling beneath the mandible, swelling of the floor of the mouth, and elevation of the tongue. The onset of total respiratory obstruction is often exceedingly sudden and dramatic. The patient may fail to complain of any appreciable respiratory embarrassment. Indeed he may not become aware of its existence until the obstruction is on the verge of becoming complete. This obstruction is caused largely by a distortion and displacement of the tongue and pharynx which are in turn the result of tension within the submandibular space. In addition, there may be a concomitant edema of the larynx. The primary object, therefore, is not merely to drain pus, but rather to decompress the submandibular space and to release the tension within it as early and as completely as possible. This can be accomplished with certainty only by transverse section of the deep fascia and the mylohyoid muscle on one or both sides, depending upon whether the infection is unilateral or bilateral. Our operative procedure consists of making an incision in the skin and platysma beneath and parallel to the horizontal ramus of the mandible. The incision is deepened to include the deep fascia, the anterior belly of the digastric muscle, and the mylohyoid muscle, all of which are divided transversely and completely. If it is suspected that the infection lies above the geniohyoid, that muscle too is divided. The floor of the submandibular space is thus laid open and the tension within it is fully released. This allows the tongue and floor of the mouth to fall back into more normal positions. The local venous engorgement is also to a large extent relieved. A division of the fibers of the mylohyoid muscle should be thorough and total, regardless of whether actual pus or edema is present. It should further be emphasized that this muscle should be transected even when pus is encountered immediately under the skin and platysma. The subcutaneous pus often communicates with the submandibular space through a narrow and tortuous tunnel. The drainage of this pus alone may therefore not appreciably change the degree of tension within the main submandibular pocket. In one of our cases the

operative procedure was terminated after the simple drainage of such a subcutaneous abscess. The respiratory difficulty was not relieved and an emergency tracheotomy had to be performed six hours after the operation. The skin incision should be planned so as to avoid injuring the mandibular branch of the facial nerve, and so that the final scar will come to lie under the chin, where it will not be conspicuous. An incision midway between the hyoid bone and the lower border of the mandible will usually meet these two objectives. For bilateral infection, a horseshoe shaped incision is made at the same level (Fig. 3). This incision, unilateral or bilateral, allows a more thorough exploration and decompression, and is attended in general with a finer cosmetic result than the midline vertical incision. The whole wound is left open and a

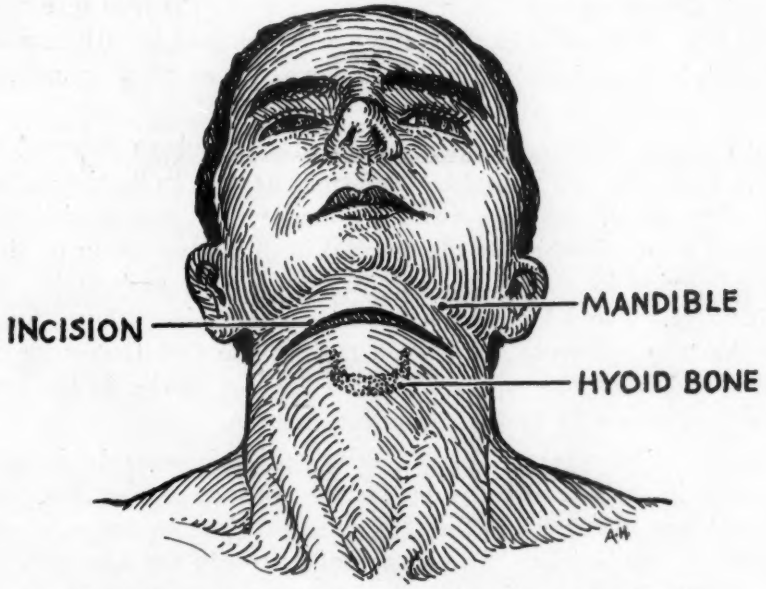

Fig. 3.—Diagrammatic sketch showing site of operative incision.

vaseline gauze pack is placed loosely into it down to the mucous membrane of the mouth. Healing takes place by secondary intention. The improvement in the general condition of the patient immediately following the opening of the submandibular space, and even before he has left the operating table, is often rapid and striking. The tenseness and anxiousness are gone, the breathing is free, and the entire physical appearance is brighter.

There are those[7, 17, 18] who advocate resection of the submaxillary gland. We have no quarrel with them, but we insist that the main objective is the adequate relief of tension in the confined space. All other considerations and technical procedures are secondary. In our group the submaxillary gland was removed only twice. Indeed, in the whole series the origin of the infection could be directly attributed to the submaxillary gland in only two instances and these, strangely enough, were

not the ones in which the glands were excised. Others[14] recommend that the drainage be instituted through the mucous membrane of the floor of the mouth. Although this approach may be possible in isolated instances, we believe that on the whole it is neither satisfactory nor feasible. Unless free pus is present, adequate exploration through the floor of the mouth may be difficult under any circumstance. This is especially true when trismus and an edematous ligneous tongue make it practically impossible to enter the mouth. In view of the current widespread and often unrestrained use of the sulfonamides, it is not surprising that these drugs have been employed in Ludwig's angina. Several reports[9, 13] have already appeared describing their successful use in this disease, and advocating them as substitutes for surgical intervention. This procedure is dangerous and does not recognize where the true threat of the disease lies. Sulfonamides may and should be used as adjuncts to the treatment, but nothing should replace immediate surgical decompression of the submandibular space.

The urgency of early surgical intervention has been referred to already. The operation should be performed as soon as possible after the diagnosis is made. In this series the decompression was carried out immediately after admission to the hospital in thirty-two cases; on the day after admission in six; on the second day in five; and on the fourth day in three. The delay, where present, was occasioned by uncertainty as to the true nature of the disease and by the fact that some of the patients had spent one or more days on another service in the hospital before they were seen by the consulting surgeon.

The operation was performed under regional novocain infiltration anesthesia in forty-two of the forty-six procedures. The novocain (½ per cent) was injected into the skin and subcutaneous tissues along the proposed line of incision. The deeper structures in the neck were found to be remarkably insensitive to pain, and the superficial infiltration was often sufficient in itself to permit the entire procedure to be carried out without discomfort. However, there was no hesitation in injecting additional novocain into the deep cervical fascia and the mylohyoid muscle when necessary. In four instances general inhalation anesthesia was used. Two were in children, five and seven years old respectively, in whom it was difficult to obtain adequate cooperation. The remaining two were in the same adult, a man 63 years of age, who had an associated suppurative cavernous sinus thrombophlebitis, and who was totally irrational and uncooperative. It cannot be too strongly urged that inhalation anesthesia should be avoided as far as possible. The struggling and spasm during the stages of induction, the increase in the secretion of mucus in the pharynx and larynx, and the relaxation of the tense and strained accessory muscles of respiration all conspire to jeopardize the freedom of the respiratory pathway. Intratracheal intubation anesthesia is often impossible due to trismus and a swollen tongue, which

mechanically prevent adequate passage of the tube. Indeed, under any circumstances a preliminary deep anesthesia is often required before intubation is possible. However, even when technically feasible, this method is not without danger, for the tube may aggravate an existing edema of the larynx and lead to its complete closure. Williams and Marcus[24] have recognized and emphasized the dangers of inhalation anesthesia and have substituted intravenous barbiturates (evipal and pentothal) as the ideal anesthetic agents. They concede that these drugs have certain disadvantages,[5, 16, 19, 20, 22, 24] but they believe that the disadvantages can be overcome. A study of their method,[24] however, with all of its complicated and extensive precautions, far from establishes the safety of these intravenous anesthetic agents. Nor does it reveal any particularly significant advantages over inhalation anesthesia. Indeed, in eight of their cases where intravenous anesthesia had been utilized, an emergency tracheotomy had to be performed on the operating table in two instances. They "feel strongly that the proper operative procedure in Ludwig's angina is too extensive to be attempted under local anesthesia."[24] Our experience certainly does not support this view.

There were two deaths in the group. At autopsy one of these patients was found to have a cavernous sinus thrombophlebitis, with pneumonia and lung abscess, in addition to the submandibular infection. The other had a dissecting aortic aneurysm which had ruptured into the thorax. This latter death cannot properly be ascribed to the angina, but inasmuch as it occurred before the patient left the hospital it is included in the mortality figures. There were no instances of mediastinitis. Pneumonia, so often recorded in other series, may in a large measure be traced to the thick mucoid secretions which lie in the pharynx and larynx, and which can be easily aspirated into the lungs in the course of a general anesthesia, inhalation or intravenous. It is our belief that the virtual absence of pneumonia in our group of cases may be directly attributed to the fact that the operations were performed early in the disease and that the procedures were carried out under local anesthesia.

CONCLUSIONS

Ludwig's angina is a surgical emergency and demands immediate operation. The cardinal symptoms appear early in the disease and can be easily recognized. They include (1) a tender swelling in the submandibular area of the neck; (2) elevation of the tongue; and (3) edema of the floor of the mouth. The high mortality in this disease is due not to some overpowering and occult virulence of the infecting organisms, but more often to a mechanical obstruction of the respiratory pathway. The primary object of the operation is to relieve and preferably to prevent this obstruction by releasing the tension within the submandibular space. This can be accomplished with safety and certainty only by complete transection of the deep cervical fascia and the

mylohyoid muscle. A thorough decompressive procedure should be performed as soon as possible after the diagnosis is made. Except in extremely extenuating circumstances, the operation should be performed under local novocain anesthesia.

REFERENCES

1. Ashhurst, A. P. C.: Ludwig's Angina, J. A. M. A. **92**: 500, 1929.
2. Ashhurst, A. P. C.: Ludwig's Angina, Arch. Surg. **18**: 2047, 1929.
3. Blassingame, C. D.: Angina Ludovici; Anatomic and Clinical Study, Arch. Otolaryng. **8**: 159, 1928.
4. Burke, John: Angina Ludovici; Translation, Together With a Biography of Wilhelm Frederick von Ludwig, Bull. Hist. Med. **7**: 1115, 1939.
5. Cameron, W. A.: Pentothal Sodium as an Intravenous Anesthetic, Anesth. & Analg. **16**: 230, 1937.
6. Coller, F. A., and Yglesias, L.: Infections of the Lip and Face, Surg., Gynec. & Obst. **60**: 277, 1935.
7. Colp, R.: Treatment of Deep Infections of Submaxillary Triangle, S. Clin. North America **13**: 315, 1933.
8. Davis, G. G.: Acute Septic Infection of the Throat and Neck; Ludwig's Angina, Ann. Surg. **44**: 175, 1906.
9. Fulghum, J. E.: Sulfanilamide Treatment of Ludwig's Angina, U. S. Nav. M. Bull. **36**: 58, 1938.
10. Grodinsky, M.: Retropharyngeal and Lateral Pharyngeal Abscess, Ann. Surg. **110**: 177, 1939.
11. Grodinsky, M.: Ludwig's Angina; Anatomical and Clinical Study With Review of Literature, SURGERY **5**: 678, 1939.
12. Grodinsky, M.: Ludwig's Angina; Retropharyngeal Abscess, J. A. M. A. **114**: 18, 1940.
13. Hendricks, W. C.: Surgery or Sulfanilamide in Ludwig's Angina, M. Rec. **150**: 415, 1939.
14. Houser, K. M.: Ludwig's Angina; Intra-oral Incision in Infections of the Floor of the Mouth, Arch. Otolaryng. **16**: 317, 1932.
15. Ludwig, W. F. von: Ueber eine in neuerer Zeit wiederholt hier vorgekommene Form von Halsentzündung, Med. Cor-Bl. d. württemb. ärtzl. Landesver Stuttg. **6**: 21, 1836.
16. Lundy, John S.: Intravenous Anesthesia, Am. J. Surg. **34**: 559, 1936.
17. Ramsdell, E. G.: Ludwig's Angina. Advantages of Submaxillary Resection, S. Clin. North America **14**: 315, 1934.
18. Rehn, E.: Die Behandlung der Ludwigsches Phlegmone durch Exstirpation der Glandula Submaxillaris, Klin. Wchnschr. **1**: 2138, 1922.
19. Ruth, H. S., Tovell, R. M., Milligan, A. D., and Charleroy, D. K.: Pentothal Sodium; Is Its Growing Popularity Justified? J. A. M. A. **113**: 1864, 1939.
20. Sise, L. F.: Clinical Evaluation of Some Nonvolatile Anesthetic Drugs, New England J. Med. **219**: 349, 1938.
21. Thomas, T. T.: Ludwig's Angina, Ann. Surg. **47**: 161, 335, 1908.
22. Van Wagenen, W. P., and Costello, C. V.: Sublingual Phlegmon; Primary and Secondary Ludwig's Angina, Ann. Surg. **87**: 684, 1928.
23. Williams, A. C.: Ludwig's Angina, Surg., Gynec. & Obst. **70**: 140, 1940.
24. Williams, A. C., and Marcus, P. S.: The Choice of Anesthesia in Ludwig's Angina, Anesth. & Analg. **20**: 160, 1941.
25. Yerger, C. F.: Ludwig's Angina, Illinois M. J. **49**: 168, 1926.

THE CLINICAL SIGNIFICANCE OF GAS IN THE GALL BLADDER

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THE circumstances under which gas appears spontaneously in the gall bladder are unusual. In rare instances it has been found at operation and at autopsy. In 1901, Stolz reported three autopsies at which gas was found in the gall bladder, and Brutt (1923) and Kirchmayr (1925) recognized cases of gaseous cholecystitis at operation. More recently a few cases have been recorded in which gas in the gall bladder and biliary ducts was visualized by x-ray. This was first reported in 1929, by von Friedrich.

There appear to be two main causes for the spontaneous appearance of gas in the gall bladder. The first of these is infection of the gall bladder with gas-forming bacteria. The second is the passage of gas from the intestine into the gall bladder through a fistula between the gall bladder and the gastrointestinal tract. Gas may enter the bile passages at operation or may be injected into them during cholangiography, but these latter sources are of relatively less diagnostic significance at present than is the spontaneous filling of the gall bladder with gas. In the last two years we have had six cases in which the spontaneous appearance of gas in the gall bladder was demonstrated by x-ray. Three of these cases were caused by anaerobic gas-forming bacteria and three by cholecystenteric fistulae. From reports in the literature and elsewhere we found twenty-one cases, eight of which fall into the first group, and thirteen into the second. The etiology and clinical course of the two types of cases are quite different. Each type requires separate consideration before the significance of gas in the gall bladder can be realized.

1. *Acute Gaseous Cholecystitis.*—This is a rare form of acute cholecystitis associated with infection of the gall bladder with gas-producing bacteria. It also has been designated as "emphysematous cholecystitis," "pyopneumocholecystitis," and "gas phlegmon of the gall bladder." The bacteria most frequently associated with this condition are gas-forming anaerobes of the Clostridium group. *Bacillus coli* is also frequently found. Acute gaseous cholecystitis is exemplified by the following cases:

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CASE 1.—D. C., a colored man 49 years of age, became ill on Dec. 27, 1939, with severe, intermittent, generalized, cramping abdominal pain which settled first in the right lower quadrant and then localized in the right upper quadrant and the right flank. He vomited three times. Two years before, the patient had had a similar but milder attack which subsided spontaneously. The general physical examination forty-eight hours after the onset of the illness was not remarkable except for the abdomen and back. There was moderate tenderness in the right upper quadrant with slight rebound tenderness, but the maximum tenderness was present in the right flank. The temperature was 101.8° F. and the pulse rate 90. The white blood count was 21,000, with 90 per cent polymorphonuclear cells. Urinalysis was negative except for a trace of albumin and glucose.

Fig. 1.—Case 1. Gaseous cholecystitis. Plain x-ray film of the abdomen showing gas in the lumen of the gall bladder forty-eight hours after the onset of acute cholecystitis. A gangrenous gall bladder was drained and the patient died about forty-eight hours after operation of a fulminating anaerobic gas bacillus infection of the peritoneum and abdominal wall.

The preoperative diagnosis was acute cholecystitis or acute retrocecal appendicitis. A plain x-ray film of the abdomen showed no evidence of renal or biliary calculi. The pyriform or roughly elliptic shadow of gas which was seen in the right upper quadrant in the x-ray film (Fig. 1) was not recognized at that time as possibly representing a gas-filled gall bladder. It was almost a year later that one of us recalled this case and the x-ray film, in connection with a study of our second case.

Operation was performed Dec. 30, 1939, under ether anesthesia, through a right rectus incision. There was a small amount of turbid fluid in the peritoneal cavity. The omentum was adherent to the under surface of the liver in the region of the gall bladder and there was some green-yellow fibrin in this area. The lower part of the abdomen and operative field were walled off with laparotomy pads. About 25 c.c. of brown-grey pus were aspirated from an abscess in the omentum immedi-

ately surrounding the gall bladder. The gall bladder was enlarged, tense, gangrenous, and jet black in color. There was no visible gross perforation. About 20 c.c. of thin turbid brown-green fluid were aspirated from the gall bladder. It contained no calculi. Cholecystostomy was performed. At the time of operation no observations for the presence of gas were made and none was noted.

On the first postoperative day the temperature rose to 104° F. and the pulse rate to 120. The abdomen became distended and the patient appeared very ill. On the following day, some edema and emphysema developed about the wound and extended over the lower thoracic wall. The patient became delirious, fell out of bed, and died a few minutes later.

At autopsy there was no evidence of injury from the fall. Extensive emphysema and edema of the right abdominal and thoracic walls were present, as well as infection of the wound, gangrene of the gall bladder, and general peritonitis.

Bacteriologic study of the contents of the gall bladder showed slender gram-positive and gram-negative rods on direct smear, and *B. coli* and large anaerobic gas-producing bacilli resembling *Cl. welchii*, on culture.

CASE 2.—E. B., a white man 59 years of age, gave a history of having had for thirty years recurring attacks of gnawing epigastric pain relieved by food and soda. One month before entry he had an attack of cramping pain in the right upper quadrant of the abdomen, with nausea and vomiting, of one day's duration. A week later he had another attack, more severe than the first, and the pain radiated through to the back. His present attack began one day before entry, with severe cramping pain in the right upper quadrant. The patient vomited once but had no chill. The upper part of the abdomen was moderately tender throughout with some guarding. A tender rounded mass was palpable beneath the right costal margin. The patient appeared to be acutely ill. The temperature was 102 degrees and the pulse rate 96. The white blood count was 13,200, with 96 per cent polymorphonuclear cells. Test of the serum amylase showed 315 units, and the icterus index was 8.7 units a short time after his entry.

The plain x-ray film of the abdomen taken Oct. 29, 1940, about twenty-four hours after the onset of his illness, showed nothing more than evidence of gas in the hepatic flexure of the colon (Fig. 2*A*). On the evening of the same day isoiodeikon was given intravenously as a test of liver function and in an attempt to visualize the gall bladder. The patient apparently had a reaction from the dye, with a chill and high fever which subsided promptly. X-ray examination the following morning showed that the gall bladder had not filled with dye, but was clearly outlined by a shadow of gas surrounded by a well-defined concentric gaseous ring (Fig. 2*B*). On the following day (Oct. 31, 1940) a film with the patient in the upright position demonstrated a fluid level below the gas (Fig. 2*D*), apparently in the gall bladder. On Nov. 1, 1940, one therapeutic dose of polyvalent gas gangrene antitoxin was given. A course of sulfathiazole was administered between November 1 and November 7. After four or five days the acute process subsided. The pain, tenderness, and spasm diminished and after the first week of his illness the patient had no complaints. The temperature gradually declined to normal on Nov. 7, 1940, and the patient remained afebrile thereafter. The leucocyte count, which never exceeded 13,400, gradually returned to normal by November 12. The stools were examined for the passage of biliary calculi, but none was found. Duodenal drainage was performed on November 23. Direct smear of the bile obtained from this drainage showed numerous large, long, gram-positive rods and, on culture, *B. coli* and anaerobic spore-forming rods of the Clostridium group were found. Frequent x-ray studies of the gall bladder showed the continued presence of gas and fluid therein, gaseous infiltration of its wall, and some extension of the

gas into the tissues surrounding it (Fig. 2*E*). After his dismissal from the hospital the patient returned at weekly intervals for x-ray examinations which revealed a diminution and shrinking in the extent of gas in the gall bladder region (Figs. 2*F*

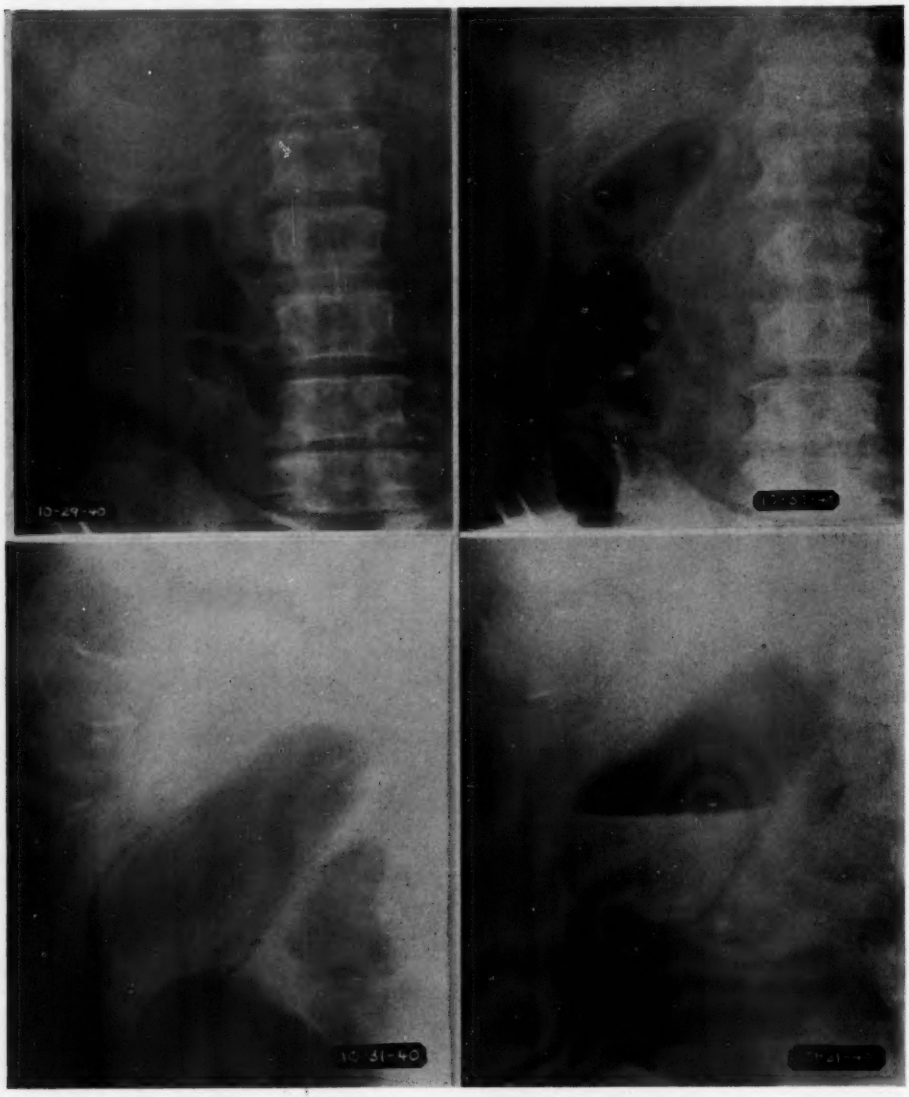


Fig. 2.

A.—Case 2. Plain x-ray film of the abdomen in a case of acute cholecystitis of about twenty-four hours' duration. No gas is seen in the region of the gall bladder, but there is some evidence of gas in the ascending and transverse colon. This is the first of a series of films taken on this patient.

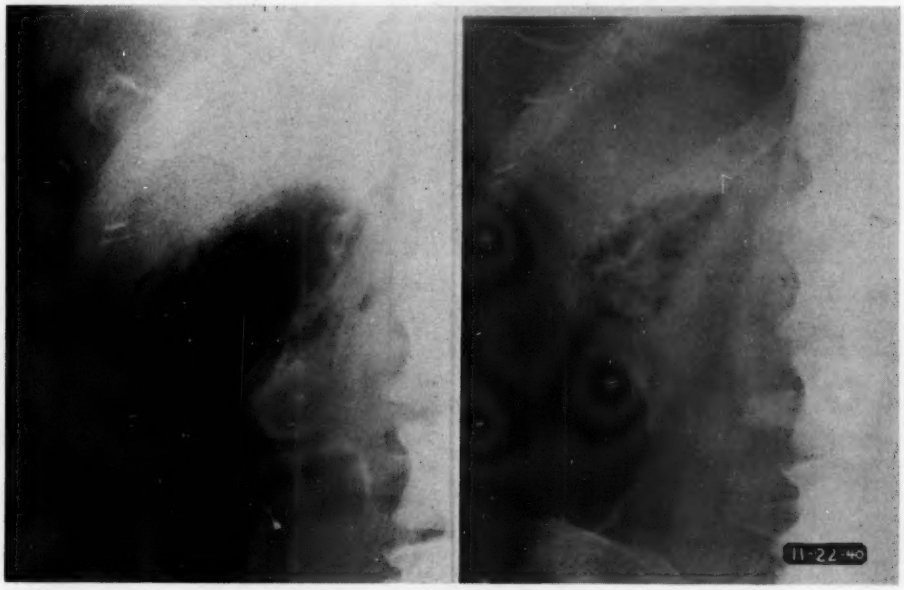
B.—Case 2. Gaseous cholecystitis. Cholecystogram taken thirty-six hours after the onset of acute cholecystitis. The shadow of gas in the upper right abdominal quadrant resembles, in size and shape, a distended gall bladder. The beginning of a concentric gas ring at the periphery of the gall bladder can be seen. This film was made with the patient in the prone position. No radiopaque dye appeared.

C.—Case 2. Film of the gall bladder taken in the prone position seventy-two hours following the onset of acute cholecystitis. The gall bladder is clearly outlined by gas. The concentric ring at the periphery is more definitely seen.

D.—Case 2. Film of the gall bladder taken on the same day as the film shown in Fig. 2*C*, with the patient upright. This demonstrates gas over fluid in the gall bladder, and gas in the wall as shown by the concentric ring.

and 2*G*) until Feb. 15, 1941, when all evidence of gas in this region had disappeared. Periodic physical examinations have shown no abnormalities.

CASE 3.—S. S., a white male 49 years of age, suffered sharp severe pain in the epigastrium at 6 p.m., March 19, 1941. He vomited several times and the pain shifted from the epigastrium to the right subcostal region where it remained as a constant severe ache. The patient had mild diabetes but had had no previous attacks of biliary disease. Marked tenderness, spasm, and rebound tenderness in the right upper abdominal quadrant were present on physical examination and the gall bladder was palpated as a large, rounded, tender mass. The temperature was 101 degrees and the pulse rate 90. There were 17,100 white blood cells, with 91 per cent polymorphonuclears. Urinalysis was negative.



E. *F.*

Fig. 2.

E.—Case 2. This film of the gall bladder was taken five days after the onset of the illness. There is evidence of extension of the gas into the surrounding tissues in some places. There is also disintegration of the original delicate layer of gas in the walls of the gall bladder.

F.—Case 2. X-ray film of the gall bladder region taken about three weeks following the subsidence of symptoms and signs of acute cholecystitis. At this time the patient was ambulatory. The film shows a loss of gas outlining the lumen of the gall bladder. The fluid level has disappeared and there is a diminution in the size of the area involved. The gas has been transformed into a cluster of bubbles of various sizes and shapes.

A roentgenogram of the entire abdomen taken on the day of entry showed a moderate amount of gas in the ascending colon and somewhat more in the transverse colon, but none was present in the gall bladder or bile ducts (Fig. 3*A*). Cholecystography (by the intravenous method) on the following day showed none of the radiopaque material in the gall bladder. Instead there was a large amount of gas and fluid in the enlarged gall bladder (Fig. 3*B*). The x-ray film taken with the patient in the erect position showed a fluid level superimposed by gas in the lumen of the gall bladder (Fig. 3*C*). Peripheral to the contents of the lumen was a continuous fine black line representing a layer of gas in the wall of the gall bladder (Figs. 3*B* and 3*C*). Twenty-four hours later the gas in the lumen had increased somewhat and extended medially into the soft tissues. The layer of gas

in the wall subsequently broke up into numerous short strands and this was accompanied by an increase in the amount of gas outside the gall bladder (Fig. 3*D*). The process apparently reached its peak about five days after the illness began. Seventeen days after the onset of the acute cholecystitis, the gas in the lumen and wall of the gall bladder had been transformed into many bubbles of various sizes. During the same period the gall bladder was shrinking in size and the pericholecystic gas in the soft tissues was disappearing (Figs. 3*A* to 3*E*).

Fig. 2*G*.—Case 2. Plain x-ray film of the gall bladder region made nine weeks after the subsidence of an attack of acute cholecystitis. At this time the patient was free from symptoms and there were no signs of cholecystitis. The shadows of gas appear in several small groups and the area of involvement is considerably diminished.

The patient was given one therapeutic dose of polyvalent gas gangrene antitoxin and a course of sulfathiazole. Duodenal drainage was performed on March 21, 1941, and, on direct smear, gram-positive rods and cocci in clumps were found; cultures showed anaerobic gas-producing bacilli resembling *Cl. welchii, B. coli* and staphylococci. The temperature and leucocyte count subsided to normal over a period of a week and the signs and symptoms of acute cholecystitis resolved rather rapidly during the same time. No calculi were found in the stools. The patient was discharged from the hospital, April 16, 1941. He has had no further symptoms.

Several cases of acute gaseous cholecystitis, similar in many ways to the three just described, have been recorded in the literature.

Simon reported a case of acute gangrenous cholecystitis in a man 32 years old. The roentgenograms in this case showed the distended gas-filled gall bladder with a fluid level and circumferential ring of gas. The diagnosis of acute gaseous cholecystitis was confirmed by cholecystectomy. Sporulating anaerobic bacteria were found in the gangrenous gall bladder.

A case of gaseous cholecystitis in a man 62 years of age was recorded by Hegner. The distended gas-filled gall bladder was visible in the

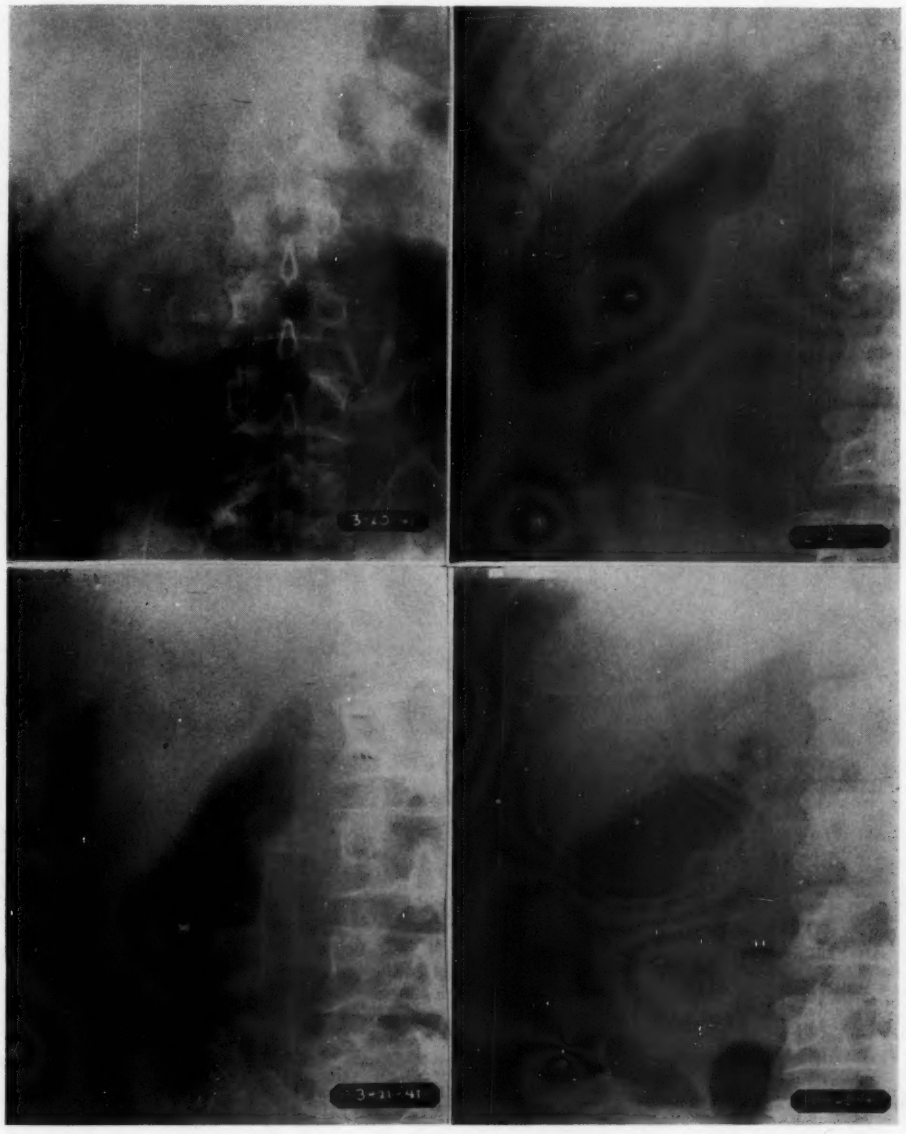


Fig. 3.

A.—Case 3. Plain x-ray film of the gall bladder region in a case of acute cholecystitis of about twenty-four hours' duration. There is no definite evidence of gas in the gall bladder.

B.—Case 3. Gaseous cholecystitis. Cholecystogram (prone position) taken about forty-eight hours following the onset of acute cholecystitis. The gall bladder is seen to be filled with gas and there is a tracing of gas in the wall of the fundus. No radiopaque material is seen. Compare with Fig. 3*A*.

C.—Case 3. X-ray film of the gall bladder (patient upright) taken on the same day as Fig. 3*B*. This illustrates a layer of fluid superimposed by gas and a thin line of gas in the wall of the gall bladder two days after the onset of acute cholecystitis.

D.—Case 3. X-ray film of the gall bladder (patient upright) taken on the fourth day following the onset of acute cholecystitis. The gas in the lumen and the fluid level in the fundus of the gall bladder are still seen. There is some evidence of extension of the gas from the wall of the gall bladder into the surrounding tissues.

plain x-ray film of the abdomen. At operation a gas-filled abscess was evacuated. Cultures of pus grew Welch's bacillus. In this case the diagnosis of acute gangrenous cholecystitis was further confirmed by autopsy.

Schmidt reported the case of a patient 37 years old, who had acute cholecystitis. The x-ray films showed the gall bladder filled with gas. Twelve days later it filled faintly with radiopaque material. This case was not confirmed by operation or autopsy. The patient recovered with medical treatment.

Wybauw described a case of acute gaseous cholecystitis in a woman 53 years old, in whom a distended gas-filled gall bladder was demonstrated by x-ray. At operation the wall of the gall bladder contained bubbles of gas.

Fig. 3*E*.—Case 3. Roentgenogram of the gall bladder about one month following the clinical subsidence of acute cholecystitis. The gas has collected into a small group or cluster of bubbles. The patient was ambulatory and free from symptoms at this time.

Berg reported two cases of acute gaseous cholecystitis but did not illustrate them.

Recently Stevenson and Baird demonstrated the x-ray films of a patient with emphysematous cholecystitis. The diagnosis was made by x-ray examination and the condition was treated by roentgentherapy. These observers also mentioned a second case, in which the treatment was surgical.

It is well known that the *B. coli* and Welch's bacillus may be cultured from the gall bladder in some cases of acute cholecystitis. It is equally

well known that these bacilli, especially the Welch bacillus, may produce gas. Other organisms may produce gas but rarely do so. Magner and Hutcheson collected statistical studies on the bacteriology of cholecystitis and noted the incidence of *B. welchii* as varying from 1 to 22 per cent in cultures from the wall of the gall bladder, and from 0.5 to 6 per cent in cultures of bile from the gall bladder. The same authors quoted the incidence of *B. coli* as varying from 4.5 to 49 per cent in cultures of the wall of the gall bladder, and from 6 to 50 per cent in cultures of the gall bladder bile from patients with cholecystitis. According to Andrews and Henry, *B. coli* is the gas-forming organism most frequently found in the gall bladder (from 11 to 16 per cent); next in frequency is *B. perfringens* (from 9 to 11 per cent of cases). Gordon-Taylor and Whitby determined that *B. welchii* was found in nearly 9 per cent of a series of gall bladders removed at operation. In this group were two cases of acute gangrenous cholecystitis in which the organism *(B. welchii)* was found in pure culture.

In the cases of acute gaseous cholecystitis discussed in this report it appears that the condition is associated with infection of the gall bladder by anaerobic gas-forming bacteria. These bacteria were found in all cases in which it was possible to obtain cultures directly at operation. The similarities of the x-ray and clinical pictures in patients who were not operated upon, together with the somewhat circumstantial evidence obtained from bacteriologic study of the duodenal drainage, appear to justify their inclusion in this group of cases.

In connection with acute gaseous cholecystitis, all of the ways in which infection may spread to and localize in the gall bladder have been considered, namely, hematogenous bacterial embolism, lymphogenous spread, direct extension from contiguous organs (for example, the gastrointestinal tract), and the influx of organisms into the gall bladder bile, either ascending from the duodenum or descending from the liver bile. At present, however, it appears impossible to determine definitely the source of the infection of the gall bladder in these cases of anaerobic gaseous cholecystitis. Speculation is invited, also, upon the difficult question as to why some gas-forming anaerobes are extremely pathogenic in certain instances, milder in others, and apparently inactive under some circumstances. The virulence of the strain of organisms and the resistance of the host are always factors which must be considered. Also, in certain diseased gall bladders there may exist a localized fertile field for the activity of gas-forming organisms; stasis, obstruction, ulceration by calculi, necrosis and anoxia caused by edema, and interference with or occlusion of the vascular supply to the gall bladder are examples. Thus, under certain circumstances of ulceration, obstruction, or interference with the vascular supply, a gall bladder which contains potentially pathogenic forms of these gas-forming anaerobic organisms may become a medium for their successful growth. That such circumstances occur rarely is fortunate.

The onset of acute gaseous cholecystitis has the clinical appearance of a severe form of acute cholecystitis. In the first few hours of a gas-producing infection of the gall bladder there is no roentgenologic evidence of its existence. It usually requires from twenty-four to forty-eight hours before sufficient gas has been produced so that it may be visualized roentgenologically. It is seen first on the x-ray film as a black area forming the outline of the enlarged distended gall bladder. Subsequently, the roentgenologic picture seems to change according to the progression or regression of the inflammatory process in the gall bladder. If the infection subsides the gas is gradually absorbed or possibly discharged through the cystic duct. This is illustrated by Schmidt's case in which the gas was said to have disappeared from the gall bladder within twelve days, the disease subsiding promptly under medical treatment. If, on the other hand, the infection continues, gaseous infiltration of the wall of the gall bladder results. Such infiltration appears as a thin dark layer of gas immediately peripheral to that in the lumen of the gall bladder. As the infectious process progresses, this thin layer of gas becomes broader and disintegrates into numerous short dark strata. At the same time, the amount of gas in the lumen of the gall bladder usually increases in volume. There is likely to be some fluid in the gall bladder in this condition and an x-ray film made with the patient in the erect position often shows a well-defined fluid level. Later in the course of the infection, the gaseous infiltration of the wall of the gall bladder extends into the surrounding tissues and the gas is seen as rounded dark areas. At this stage there is probably pericholecystitis and there may be pericholecystic abscesses containing gas. In the cases of acute gaseous cholecystitis in which the patients recovered, the findings described above were followed by x-ray evidence of a very gradual absorption of the gas. That in the lumen of the gall bladder lost its contour first; there followed shrinkage and disruption of the layers of gas in the wall and lumen of the gall bladder into bubbles of various sizes. These were seen in the x-ray films as clusters of more or less circular dark areas. Evidence of gas in the tissues could be demonstrated by x-ray long after clinical evidence of acute cholecystitis had disappeared. Gas was not seen in the bile ducts in the roentgen-ray films of any patient with gaseous cholecystitis. The two patients treated conservatively have remained well.

The management of cases of acute inflammatory disease of the gall bladder accompanied by x-ray evidence of gas in the gall bladder deserves special consideration. Because of the rarity of the spontaneous occurrence of gas in the gall bladder, no surgeon has had enough experience with this interesting finding to be able to draw any final conclusions about it.

It is difficult to outline a general policy for the management of acute cholecystitis. As a rule, we treat acute cholecystitis conservatively and

prefer to carry out surgical procedures at some elected time after the acute process has subsided. Special consideration, however, is given to the individual problem presented by each patient with cholecystitis and, actually, we often find it necessary to operate early for acute cholecystitis. Each case of acute gaseous cholecystitis merits particularly careful clinical management. The risk of disrupting and disseminating a more or less localized gas bacillus infection by operative manipulations must be weighed against the possibility of perforation of the gall bladder into the free peritoneal cavity. Our unfortunate experience in our first case of this type made us feel that, in future cases, a conservative or expectant course should be pursued even more persistently than usual. The patient described in Case 1 died of a fulminating gas bacillus infection of the abdominal and thoracic walls and peritoneum following cholecystostomy for acute gangrenous gaseous cholecystitis of about 60 hours' duration. He was operated upon because we could not eliminate the possibility of a high retrocecal appendicitis and because we did not recognize at the time that the shadow of gas in the x-ray film represented a distended gall bladder filled with gas. Our second and third cases of acute gaseous cholecystitis were managed with even greater than usual conservatism because of the unfortunate experience with this first patient. We also believe, both because of our experience and the reports of other observers who have seen rare cases in which there was dissemination of gas bacillus infection following operations on the biliary tract, that the usual interval cholecystectomy should not be performed in cases of gaseous cholecystitis. Every effort will be made to avoid operation on the biliary system in the event of later recurrence of symptoms. Though it is scarcely permissible to express an opinion based on such a small experience with acute gaseous cholecystitis, we are inclined to believe that conservative management with supportive treatment should preferably be employed during the acute phase of this disease, and that both early and interval operation should be avoided if possible. It should be mentioned, however, that other observers have reported successful operations in cases of acute gaseous cholecystitis. X-ray therapy has been used in at least one case. The treatment of acute gaseous cholecystitis with polyvalent anaerobic antitoxin, chemotherapy, or x-ray therapy may be indicated, but the efficacy of such measures will probably be as difficult to evaluate in these cases as in other anaerobic gas bacillus infections.

2. *Cholecystenteric Fistulae.*—These are occasionally associated with the spontaneous appearance of gas in the gall bladder. The condition usually demands investigation because of one or more episodes of acute cholecystitis or cholangitis. The x-ray films taken in these cases have shown evidence of gas in the gall bladder and bile ducts in a few instances. This gas probably comes from the intestinal lumen. The following case reports exemplify cholecystenteric fistula with gas in the gall bladder and bile ducts:

CASE 4.—M. S., a woman 35 years of age, had had indigestion and discomfort in the right upper abdominal region all of her life. At operation four years previously, the gall bladder had appeared to be normal, but there was a large cyst of the common duct that was not definitely identified as such at the time. The cyst was drained and an external biliary fistula resulted. Three months after the first operation laparotomy was performed again. A large lycopodium granuloma was removed and an anastomosis between the common duct and the duodenum was performed. The patient remained free from symptoms until about four months before her present entry, when she began to have transient attacks of nausea and pain in the right upper quadrant of the abdomen. She had many such attacks and suffered a chill with one of them. On physical examination no abnormal findings were noted. There was a healed scar in the right upper quadrant. The laboratory findings were within normal limits and the patient was afebrile.

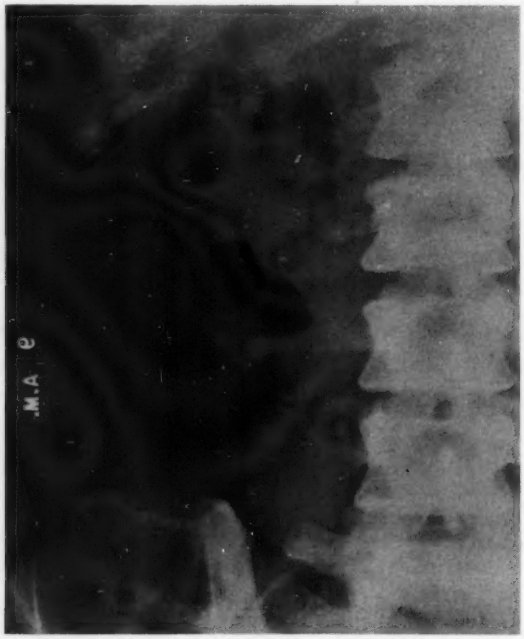
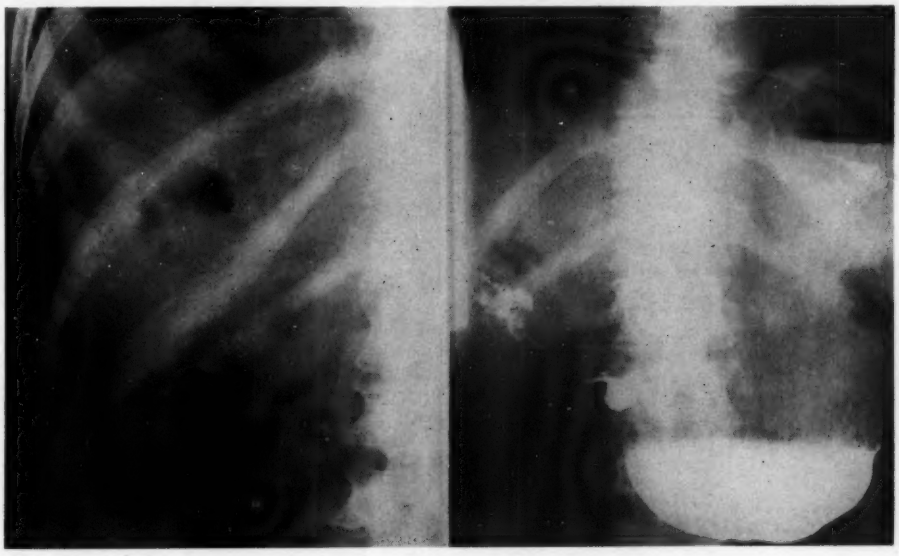


Fig. 4.—Case 4. Choledochoenteric fistula. Roentgenogram of a patient who had had a choledochoduodenostomy four years previously. In the last four months she had had attacks of pain in the right upper abdominal quadrant accompanied by nausea and chills. The gas-filled gall bladder can be seen.

Cholecystography was done by the intravenous method. The gall bladder was not demonstrated by the opaque material but in all the films appeared a shadow of gas the size and shape of the gall bladder (Fig. 4). A barium meal showed some reflux of barium into the common duct. Operation was not advised.

CASE 5.—F. P., a woman 54 years of age, had had a cholecystostomy two years previously for recurring episodes of cholecystitis with colic, of twenty-four years' duration. She was then well until eight months before entry, when she began to have attacks of severe pain in the right upper abdominal quadrant with chills, nausea and vomiting, fever to 105° F. at times, and jaundice. She lost fifty pounds in weight in eight months. At the time of entry she was not jaundiced. She was obese and there was moderate tenderness beneath the right costal margin. The laboratory findings were not remarkable.

The gall bladder did not fill with the opaque solution given for cholecystography, but a collection of gas was seen in the gall bladder (Fig. 5*A*). A barium meal showed 95 per cent gastric residue after three hours. A small amount of barium was seen in the gall bladder (Fig. 5*B*) and the duodenal bulb did not fill. At operation a very hard mass, about 6 cm. in diameter, was found in the region of the pylorus and gall bladder. It was bound down by firm scar tissue to the stomach, liver, duodenum, and transverse colon. In an attempt to free this mass, a fistula between the gall bladder and stomach was encountered. The gall bladder contained numerous small faceted calculi. A biopsy of the tissue was taken and a report of adenocarcinoma was made. Because of the poor condition of the patient the opening in the stomach was sutured, an anterior gastroenterostomy was done and the gall bladder was drained. The patient died of peritonitis; autopsy was not granted.



A. *B.*

Fig. 5.

A.—Case 5. Cholecystogastric fistula. X-ray film showing gas in the gall bladder of a patient who had a cholecystogastric fistula demonstrated at operation. The cause of the fistula was malignant ulceration of the stomach involving the gall bladder.

B.—Case 5. Following a barium meal, the gall bladder shown in Fig. 5*A* is partly filled with barium and gas.

CASE 6.—A. S., a woman 41 years of age, complained of painless jaundice of twelve days' duration. At operation, May 31, 1940, carcinoma of the head of the pancreas was found. A palliative cholecystoduodenostomy was done.

One and one-half years later the patient returned to the University Hospital. At that time she complained of recurrent episodes of nausea and severe pain in the right upper quadrant of the abdomen. The pain radiated to the back and was accompanied by a sensation of epigastric distention. This attack was of two weeks' duration. There was tenderness throughout the abdomen, most acute in the right upper quadrant. While the patient was in the hospital she had repeated attacks of severe pain in the right upper quadrant, with vomiting. Her temperature rose to 102.2° F. on several occasions.

X-ray examination showed the gall bladder, common duct, and hepatic ducts to be filled with gas. A barium meal showed marked contrast between the intestine

and the gas-filled bile ducts but none of the opaque material entered the bile ducts. The patient died two months later. At autopsy carcinoma of the ampulla of Vater with extension into the pancreas was found.

Several cases of cholecystenteric fistula with x-ray evidence of spontaneous filling of the gall bladder or bile ducts with gas, similar to the three cases just described, are reported in the literature.

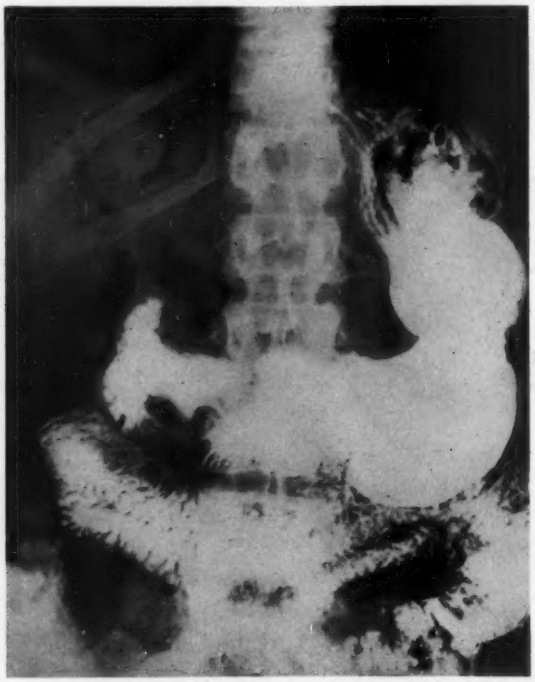


Fig. 6.—Case 6. Cholecystoduodenal fistula. Roentgenogram showing gas in the gall bladder and bile ducts of a patient who had had a cholecystoduodenostomy for carcinoma of the ampulla, one and one-half years previously.

Von Friedrich described two cases in which the gall bladder, common duct, and hepatic ducts were filled spontaneously with gas. One of the patients had previously had a surgical cholecystoduodenostomy for carcinoma of the pancreas. The second patient had a spontaneous cholecystduodenal fistula associated with cholelithiasis. In both cases attention was directed to the condition because of episodes of acute cholangitis, and the presence of gas in the gall bladder and ducts was discovered by x-ray examination. Henry described a case of choledochoduodenal fistula with gas in the common, hepatic, and cystic ducts. Pohlandt reported a case of cholecystogastric fistula secondary to cholelithiasis in which gas was found in the gall bladder, common duct, and hepatic ducts. Powers described three cases of cholecystoduodenal fistula caused by cholelithiasis, in which gas was demonstrated in the biliary ducts. Berg reported six cases of fistula between the bile ducts and intestine, in which gas was found in the biliary tract. Three of them were caused by chole-

lithiasis, two were associated with duodenal ulcer, and one was caused by carcinoma of the stomach.

The simplest and most obvious way that gas may enter the bile ducts from the intestinal tract is through a surgical anastomosis between them. Spontaneous fistulae between the gall bladder and various parts of the intestinal tract, notably the duodenum, stomach, and colon, are known to occur and they also are potential sources of gas in the gall bladder and bile ducts. The possibility of regurgitation of gas from the duodenum into the biliary ducts and gall bladder by way of the ampulla must also be considered in connection with this phenomenon. With our present information, it is impossible to say whether or not it has occurred. Berg attempted the retrograde filling of the bile ducts with air and gas, but without success. The rare instances in which barium has been reported to have passed from the duodenum into the bile passages at examination by barium meal, and the isolated cases in which foreign bodies have undoubtedly entered the gall bladder from the intestinal tract through apparently normal bile passages, make the possibility of this source of gas in the bile passages a matter for consideration.

It is probable that the gas appearing in the bile ducts and gall bladder comes from the gases that normally exist in the intestinal lumen, and that it enters through the stoma of the cholecystenteric communication. The possibility must be considered, however, that anaërobic gas-forming bacteria, introduced into the gall bladder and bile passages through a fistulous opening in the gastrointestinal tract, might grow in the bile passages and produce gas in a manner similar to that described above for the first type of case (gaseous cholecystitis). No record was found of a proved case of this type.

Under circumstances other than surgical anastomosis between some part of the bile passages and the gastrointestinal tract, the presence of gas in the gall bladder or bile ducts may be strongly suggestive of spontaneous fistula between these tracts. In such cases the patient's course often suggests chronic disease in the gall bladder with episodes of severe cholecystitis, cholangitis, colic, or intestinal obstruction. Since these patients usually have had disease of the gall bladder for some time, it is not surprising that the gall bladder tends to be either normal in size or somewhat smaller than usual, and that the bile ducts appear somewhat larger than would be expected normally. The commonest cause of these fistulae is probably calculous cholecystitis with infection and ulceration of the gall bladder. Rarely, peptic or neoplastic ulceration may produce cholecystenteric fistula. Further confirmation of the presence of such a fistula may sometimes be accomplished by the use of barium enema or barium meal. The discovery in the stool of very large calculi of biliary origin is also valuable confirmatory evidence of cholecystenteric fistula.

When the gall bladder or bile ducts are filled with gas they may be visualized by x-ray examination and this serves as a valuable means of

establishing the diagnosis of cholecystenteric fistula. In these cases the bile ducts as well as the gall bladder are usually, though not always, outlined in gas.

The treatment of patients with cholecystenteric fistula in which there is evidence of communication between the bile passages and some portion of the gastrointestinal tract, as manifested by gas in the gall bladder or bile ducts, is essentially the same as that outlined elsewhere for such fistulae. Expectant or conservative treatment during the acute phase would, therefore, be in order, unless intestinal obturation by a biliary calculus causing intestinal obstruction occurred. Many of these fistulae have been reported to have healed spontaneously. If operation must eventually be done in a case of cholecystenteric fistula, a quiescent period will probably offer a more favorable opportunity to correct the lesion and effect repair.

3. *Differential Diagnosis.*—The differential diagnosis of cases in which gas is found in the gall bladder on x-ray examination is usually not difficult. The clinical picture of the onset of acute disease of the biliary tract in the two types of cases in which gas appears spontaneously in the gall bladder may be somewhat similar at the onset of the condition. The x-ray findings and the subsequent clinical and roentgenologic courses of the two types of conditions, however, are usually different. In a case of cholecystenteric fistula with gas in the gall bladder, the gall bladder is likely to be normal in size, or small, and the bile ducts as well as the gall bladder contain gas visible on x-ray examination. In cases of infection of the gall bladder with anaerobic gas-forming organisms the x-ray film usually shows an enlarged or distended gas-filled gall bladder without evidence of gas in the ducts. In the anaerobic type a fluid level may be seen in films taken in the upright position. In addition, a ring of gas outlining the gall bladder is usually observed. Neither of these has been found in cases of fistula. The changes suggesting disintegration of the gas in the gall bladder, its spread into surrounding tissue, and later absorption are characteristic of anaerobic gas-producing infections of the gall bladder and are not found in cases of cholecystenteric fistula. The use of barium contrast medium may help to confirm the presence of fistula.

The x-ray appearance of the circumferential ring of gas present in acute gaseous cholecystitis may be simulated by lipomatosis of the wall of the gall bladder. Kommerell reported such a case. The reason for the similarity is that lipomatous tissue, possessing a density less than that of surrounding viscera, may also appear black against a light background on the x-ray film, just as gas does. This, however, can be differentiated from gaseous infiltration by the changes which occur from day to day in the cases of gas infection, while lipomatosis of the wall of the gall bladder maintains a uniform appearance. Furthermore, there will be no gas or fluid level in the gall bladder in the case of lipomatosis.

SUMMARY

There are two types of pathologic conditions in which the spontaneous appearance of gas in the gall bladder may be demonstrated roentgenologically. The first occurs as a result of an acute infection of the gall bladder with anaerobic gas-forming bacteria. The second is the result of an abnormal communication between the gall bladder or bile ducts and some part of the gastrointestinal tract. Air may enter the gall bladder or bile ducts during surgical procedures on those structures or during cholangiography, but at the present time this source is considered to be of little diagnostic significance.

In every case reviewed in this report an episode of acute cholecystitis led to the discovery of gas in the gall bladder. X-ray examination is essential for the diagnosis. The x-ray and clinical findings in both types of cases are described and illustrated.

Conservatism is the keynote in the therapeutic management of the cases in which gas in the gall bladder results from anaerobic gas-producing infection. It also seems desirable to pursue an expectant course in cases in which a cholecystenteric fistula is suggested by a gas-filled gall bladder, allowing opportunity for the acute inflammatory process to subside and a chance for the fistula to close spontaneously before operation is undertaken.

REFERENCES

1. Andrews, E., and Henry, L. G.: Bacteriology of Normal and Diseased Gallbladders, Arch. Int. Med. **56**: 1171, 1935.
2. Berg, H. H. (Hamburg, Germany) quoted by Rigler, L.: Report of the Fifth International Congress of Radiology in Chicago, Ill., SURGERY **3**: 159, 1938.
3. Berg, H. H.: Gasfüllung der Gallenwege, Fortschr. a. d. Geb. d. Röntgenstrahlen **61**: 1-9, 1940.
4. Brutt, H.: Gasbacilleninfektion des Pankreas und Pankreasnekrose, Virchow's Arch. f. path. Anat. **246**: 33-41, 1923.
5. Eliason, E. L., and Stevens, L. W.: Spontaneous Internal Biliary Fistula, Am. J. Surg. **51**: 387-392, 1941.
6. Gordon-Taylor, G., and Whitby, L. E. H.: A Bacteriological Study of Fifty Cases of Cholecystectomy With Special Reference to Anaerobic Infections, Brit. J. Surg. **18**: 78-82, 1930-31; The Incidence of Anaerobic Infections in the Gallbladder **19**: 619-621, 1931-32.
7. Hegner, C. F.: Gaseous Pericholecystitis With Cholecystitis and Cholelithiasis, Arch. Surg. **22**: 993, 1931.
8. Henry, Lucas: Hepatic and Cystic Ducts Visualized by Spontaneous Filling With Gas and Barium, Radiog. & Clin. Photog. **9**: 9-10, 1933.
9. Judd, E. S., and Burden, V. G.: Internal Biliary Fistula, Ann. Surg. **81**: 305-312, 1925.
10. Kirchmayr, L.: Ueber einen Fall von Gasbrand der Gallenblase, Zentralbl. f. Chir. **52**: 1522, 1925.
11. Kommerell, B.: Lipomatose der Gallenblase im Röntgenbild, Fortschr. a. d. Geb. d. Röntgenstrahlen **61**: 308-309, 1940.
12. Magner, W., and Hutcheson, J. M.: Cholecystitis. A Bacteriological and Experimental Study, Canad. M. A. J. **27**: 469-477, 1932.
13. Pohlandt, Klaus: Gallenblasen-Magenfistel nach Steindurchbruch, Bruns' Beitr. z. klin. Chir. **159**: 138-147, 1934.
14. Powers, R. A.: Air in the Hepatic Ducts; an X-ray Sign of Biliary Fistula, Radiology **27**: 474-478, 1936.

15. Schmidt, E. A.: Emphysematous Cholecystitis and Pericholecystitis, Radiology **31**: 423-427, 1938.
16. Simon, Joseph: Le Pyopneumocholécyste et son Diagnostic Radiologique, Presse méd. **40**: 1938-1940, 1932.
17. Stolz, A.: Ueber Gasbildung in den Gallenwegen, Virchow's Arch. f. path. Anat. **246**: 33-41, 1923.
18. von Friedrich, L.: Luft in den Gallenwegen als diagnostisches Merkmal, Fortschr. a. d. Geb. d. Röntgenstrahlen **39**: 616-619, 1929.
19. Wakefield, E. G., Vickers, P. M., and Walters, W.: Cholecysto-enteric Fistulae, SURGERY **5**: 674-677, 1939.
20. Walters, W., and Snell, A. M.: Diseases of the Gallbladder and Bile Ducts, Philadelphia and London, 1940, W. B. Saunders Co., pp. 61, 127-128, 162-164.
21. Wybauw, L.: Image Vesiculaire Inhabituelle, J. Belge Gastro-enterol. **4**: 123-125, 1936.

THE SURGICAL TREATMENT OF CARCINOMA OF THE STOMACH IN AGED INDIVIDUALS

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DURING the past decade there has been a growing interest in the surgical attack upon carcinoma of the stomach. The use of x-ray therapy alone, which at first seemed to offer sufficient palliation to justify its application at least in those cases which were considered inoperable, has proved to be disappointing and it has become obvious that the only hope in obtaining five-year or permanent cures, or definite palliative relief lies in gastric resection.

The more or less hopeless attitude toward radical gastric resection which was present in the 1900's was largely based upon a high mortality rate and a belief that actual help to the patient did not justify the use of this dangerous procedure. But with the passage of time, cases are now known to have survived ten, twelve, fifteen, twenty and twenty-two years following the radical operation. Actually, the number of cases reported is small but the fact remains that these people lived because of the operation and that alone. It is true that some of these long-lived cases died eventually of metastases distant in location from the gastrointestinal tract. Thus, some hopelessness still persists today, but the present results do not support such profound pessimism. Cooper,* in a recent article, states that 44 per cent of operable cases have survived five years. The cases which died before the expiration of five years in large proportion were improved and their symptoms greatly relieved for from one to four years. When one realizes that the patients who were explored but not subjected to resection had to endure nine months of starvation, debility, and weakness before death, the chance for cure or five-year cure, or even several years of comfortable living should not be disregarded. It must be pointed out that those patients who survive resection even though cure is not to be expected, die within four years postoperatively, but their lives prior to death are often normal and their death, due to metastases to the lung or liver or generalized carcinomatosis, is frequently not attended with prolonged starvation.

Physicians who are familiar with the natural course of the disease know that carcinoma in the aged individual exhibits a slower growth

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*Cooper, W. A.: Problem of Gastric Cancer, J. A. M. A. 116: 2125-2129, 1941.

of the original tumor, a less rapid advance of the metastatic lesions and, therefore, a longer course before the disease advances sufficiently to cause the death of the individual. Therefore, it would seem that aged individuals have a better chance for permanent cure or at least more prolonged palliation than younger people. It is because of this that we have renewed our interest in attacking these serious lesions in the aged, as well as in the young or middle age group.

TABLE I

STATISTICS ON GASTRIC CANCER IN PERSONS OVER 60 YEARS OF AGE (1932-1940)

	NUMBER OF CASES	OPERATIVE DEATHS
No operation	49 (47.0%)	
Explored, but not resected	23 (22.0%)	2 (8.7%)
Explored and resected	11 (10.6%)	1 (9.0%)
Palliative gastric resection	6 (5.9%)	3 (50.0%)
Palliative gastroenterostomy	11 (10.6%)	5 (45.5%)
Miscellaneous operations:	4 (3.9%)	2 (50.0%)
2 gastrostomies (1 operative death)		
1 total gastrectomy (1 operative death)		
1 gastroenterostomy (no operative deaths)		
Total	104	13 (23.6%)

TABLE II

STATISTICS ON ALL GASTRIC CANCER CASES (1932-1940)

Total number of cases			289
Patients not operated upon			99
Operations: (Two patients had 2 operations)			192
	NO.	OPERATIVE DEATHS	
Explored	98	8 (8.2%)	
Gastric resection	42	5 (11.9%)	
Palliative gastric resection	20	3 (15.0%)	
Palliative gastroenterostomy	23	6 (26.0%)	
Miscellaneous	9	6 (66.7%)	
Patients dead		(82.4%)	238

In Tables I and II are collected the data on 289 cases of gastric cancer, 104 of which involved patients over 60 years of age. Attention is called to the fact that the mortality in the resected cases of persons over 60 years is 9 per cent as against 11.9 per cent for the entire group. The mortality is higher in the aged group on whom palliative gastric resection is performed. Also, palliative gastroenterostomy is not only attended by a high mortality rate but is notably unsuccessful in relieving the patient.

The present low mortality rate deserves attention. In the 1920's the mortality rate in gastric resection for carcinoma ranged from 25 to 40 per cent. A study of the chief causes of death responsible for this high mortality rate shows that they were pneumonia, evisceration, pneumonia plus evisceration, general debility, and circulatory accidents. The in-

telligent use of sulfapyridine combats pneumonia to the point where it is now much less dangerous a complication, and although all cases cannot be saved by its use, the number of deaths due to postoperative pneumonia is decreasing. Also, in combatting pneumonia there is less coughing, less dyspnea, less abdominal distention, and consequently less strain on the sutured wound, and therefore this probably reflects itself locally by decreasing the number of cases of evisceration. Through-and-through silver wire in approximating the wound also is a safeguard against evisceration for it tends to maintain the integrity of the wound in the presence of infection. Postoperative embolism is still an important factor, and as the other complications decrease in severity it is more apparent as a cause of death than it was previously. In this age group we have kept the patients in bed immediately following operation, but now we often allow them out of bed and walking in three or four days following operation. Whether this prevents embolus formation is not proved, yet the fact that not one of these patients died of embolus or had clinical pulmonary emboli suggests that this treatment may have added something to their prevention. Also, with the increasing use of heparin it is to be hoped that this very serious complication may be limited still further.

It is to be noted that in the pre- and postoperative phase measures are carried out which seem to be very helpful in preventing serious trouble. In patients with carcinoma one is impressed with the fact that there is a low acidity and that there is a heavy bacterial growth on the ulcerated lesion. Consequently, wound infection and peritonitis are much more commonly seen in patients with carcinoma as compared with those with ulcer, in whom the same operation is often used. More attention should be given to the fact that the carcinomatous stomach is an infected stomach. Wangensteen had developed a closed technique for gastric resection because of the high incidence of infection. The measures that may be used to help prevent serious infections are lavage decompression when obstruction is present, and the administration of sulfaguanidine or sulfadiazine previous to the operation. The results of this therapy will probably show a small incidence of infection. Full vitamin balance can now be obtained in a very short time and should be utilized in these cases preoperatively. Fluid balance in the dehydrated patient and high caloric intake by supplementary glucose, clyses and infusions are also important. A study of the circulatory system of these aged individuals and a correction by the use of digitalis and other drugs if necessary is a valuable preoperative aid. It is important in the preoperative phase that the patient be ambulatory in order to prevent stasis of the circulation.

Diagnostic Aids.—It is obvious that early operation in aged individuals is as essential as in other groups if good results are to be obtained. The history of the patient is often the most important and

effective lead to an early diagnosis. The insidiousness of the disease and the apparent neglect of the individual to become interested in his symptoms are well known. The physician also may not be impressed because the symptoms of loss of appetite, anorexia and weakness, may be considered the result of age rather than the manifestations of an organic lesion. The physical examination in the early stage may fail to reveal anything of note and the physician may be deceived because the physical examination seems negative. Any patient with a history of loss of appetite, aversion to food, loss of weight, and weakness must be suspected of having gastrointestinal carcinoma until proved otherwise if we are to diagnose the early cases. Laboratory aids are helpful but not in themselves positive. Gastric analysis in about 90 per cent of the patients shows a low gastric acidity, but there are 10 per cent in whom the acid may be high. Bacteriologic studies of the gastric juice are helpful. Patients with ulcer very seldom show a high titer of bacteria, but in carcinoma the Boas-Oppler bacillus as well as numerous pyogenic organisms can be found in the gastric juice. The finding of blood in the gastric juice may or may not be helpful. Stool examination reveals occult blood in a high percentage of the cases, but this is not always present. X-ray examination is extremely helpful, but one must not depend on the x-ray examination alone because in a very small early lesion, particularly on the greater curvature but also in the prepyloric region and upon the lesser curvature, it may be overlooked in the early stages. The x-ray examination also may be misleading in that it may appear to show a hopeless cancer of the stomach which at operation is demonstrated to be an early resectable lesion. Therefore, x-ray must not be relied upon completely as to the presence or operability of gastric carcinoma. Gastroscopic examination which has been so enthusiastically advocated by Schindler and has been adopted in most of the clinics in the country also is a valuable adjunct, but again has its limitations. The prepyloric region of the stomach can quite accurately be examined, but there are parts of the lesser curvature which cannot be seen even though the growth at that site may be large. Gastroscopists, as a result of their examinations, have stated that a lesion was hopelessly inoperable when at operation we have been able to do a successful radical resection.

In reviewing the diagnosis of early carcinoma as determined by our experience, it is apparent that neither a careful history or physical examination nor any of the laboratory aids are individually conclusive but, taken together, serve to establish the diagnosis of cancer in a fairly high proportion of cases. In a small proportion of cases, exploratory laparotomy appears still to be a justifiable procedure.

Anesthesia.—The choice of anesthesia in this group of cases is difficult to make and varies in the hands of different operators because no one rule can be applied to all cases. Local anesthesia can be used in

some, but it must be borne in mind that certain of these elderly individuals will show a definite reaction to the use of novocain, and we have had to abandon the operation because of such reactions in two patients. Gas-ether anesthesia raises the blood pressure and may be a contributory factor in some of the vascular accidents, therefore it has not been generally used. Open-drop ether has been found to be satisfactory even in those cases with cardiac involvement. We have felt that avertin is too depressing in these individuals, and that spinal anesthesia with its resultant lowering of the blood pressure in a great number of cases may be a factor contributing to vascular disturbances in patients of this age group. Consequently, local anesthesia, if it is possible to use it, or open-drop ether are in our experience the anesthetics of choice.

Procedure.—The operative procedure used is the usual radical resection either of the Billroth type II when the tumor is small and in the pyloric region or of the Polya-Hofmeister type, making the anastomosis either retro- or antecolic depending upon the anatomic relations that exist. The Hofmeister operation has been a very successful one in our hands. We have not used the closed type of operation in any of our cases.

Postoperative Care.—For a period of twenty-four to forty-eight hours nothing is given by mouth and the fluid balance is maintained by clyses and infusions. One ounce of water by mouth per hour is begun between twenty-four and forty-eight hours postoperatively and this is gradually increased until the patient is taking a six-feeding soft diet at the end of one week. In some cases we have increased this much more rapidly without ill effect. With through-and-through wires present in the wound, one is able to allow the patient out of bed as soon as the postoperative reaction has subsided. It is important to continue vitamin intake as well as to maintain the fluid balance. The sulfonamide therapy usually is continued four to five days postoperatively, provided there are no signs of toxicity, and then it is abandoned. The silver-wire stitches are removed from the fifteenth to twentieth day, and the patient is discharged from the hospital on any balanced diet that he desires. It seems obvious that the measures that are now utilized in the pre- and postoperative phases are contributing to a low mortality rate.

DISCUSSION OF CASES

CASE 1.—Dr. H., aged 68 years. A nine-month history of anorexia, loss of weight, loss of energy, and general malaise had been recognized by this physician as symptoms of carcinoma of the stomach. He was opposed to operation and did not consult a physician until at the end of nine months the symptoms, plus vomiting, became so marked that he begged for any relief that could be offered. The physical examination and all objective tests indicated that the lesion was hopelessly inoperable with peritoneal carcinomatosis. Exploratory laparotomy was performed and the

stomach was found to be completely involved. There were metastases in the liver, omentum, regional glands, and peritoneum. Because of the distressing vomiting, a site on the anterior aspect of the stomach was chosen for gastroenterostomy, which did not function satisfactorily, and the patient succumbed on the twelfth day of bronchopneumonia. The case demonstrates a physician who thought it was hopeless to ever have gastric resection performed for carcinoma of the stomach and chose to die rather than have the operation, but became so miserable that he begged for operation at a time when all chance of recovery or palliation was gone.

Fig. 1.—Case 1., Dr. H.

CASE 2.—Mr. S., aged 60 years. This was a patient with severe cardiac disease, who had been treated at the Rockefeller Institute for a period of over two years for intermittent cardiac decompensation. For ten months previous to admission he had developed, along with his cardiac symptoms, anorexia, weight loss, and weakness. Carcinoma of the stomach was suspected but his physicians did not consider operation because of his severe cardiac disease. At the end of ten months of these symptoms, however, the cardiac phase had improved and it appeared that he was dying now from starvation. X-ray showed a large lesion in the prepyloric region which was considered to be so advanced that operation was thought to be a mere gesture. Under local anesthesia supplemented by open-drop ether, exploration was performed. The lymph nodes along the lesser curvature, as well as several places in the liver, contained small metastases. Gastric resection was done and his postoperative course

was uneventful. He lived without gastric symptoms for two years and four months following the operation. One cannot say that he did not die of carcinoma, but his palliation was real.

CASE 3.—Mrs. D., aged 65 years. This woman had had a cholecystectomy for gallstones with biliary colic three years previous to the onset of the gastric symptoms. While performing the cholecystectomy the operator explored the abdomen and found nothing pathologic in the stomach or other organs, with the exception of the gall bladder. Two years later this patient began to complain of indigestion of the type which she herself felt was different from the indigestion that attended the gall bladder disease and she immediately sought the advice of her physician about it. Her family physician, knowing that her original trouble was gallstones, thought she might be having indigestion associated with biliary tract disease, corrected her

Fig. 2.—Case 2., Mr. S.

diet, and waited for one month. At the end of this time the symptoms persisted in spite of the dietary correction, so he made laboratory studies which showed a low gastric acidity, occult blood in the stools, and a small but definite neoplastic involvement of the prepyloric area in the x-ray. After the proper preparation, exploration was done under ether anesthesia. The lesion was movable and there were a few small involved glands on the lesser curvature. A Hofmeister resection was easily performed. There was a mild wound infection but no fear of evisceration because of the presence of silver wires. Now, twelve months following the operation she is in good health, but having some difficulty with eating large amounts comfortably.

Fig. 4.—Case 5., Mrs. B.

Fig. 3.—Case 3., Mrs. D.

CASE 4.—Mrs. McD., aged 70 years. This is a woman who had been perfectly healthy all her life and had never had to consult a physician, who began to have anorexia, loss of weight, and weakness fifteen months before admission. One month before admission, while vacationing in Vermont, she had a large gastric hemorrhage, evidenced by the vomiting of large amounts of blood, as well as passing tarry stools. She recovered from the hemorrhage, and on examination showed loss of weight, anemia, a large mass in the left upper quadrant, and also inability to take at that time a teaspoonful of water without regurgitation. The gastric juice showed

Fig. 5.—Case 6., Mrs. S.

fresh blood and no acid. The stools were positive for blood and the x-ray showed a huge lesion involving almost the entire stomach. On exploration under ether anesthesia there was a huge carcinoma involving all of the stomach except about two inches in the cardiac region. The lymph nodes along the lesser curvature were extensively involved. One or two metastatic areas in the liver were found. Because of her inability to take even water, a gastric resection was done, but it was necessary to leave some of the involved glands. She developed bronchopneumonia on the forty-eighth hour, was given sulfapyridine, and promptly recovered. A mild infection of the wound developed but this cleared upon drainage. This patient lived six

months following the operation, and up to two weeks before her death was able to eat all kinds of soft foods with comfort.

CASE 5.—Mrs. B., aged 58 years. This patient had suffered from dyspepsia for ten years. Three years before admission her indigestion became more marked, she lost her appetite, lost weight, and was unable to eat even small amounts of food without feeling "full." She did nothing about this until she had lost twenty pounds in weight and became so weak that she could not do her housework. Physical examination showed only loss of weight and tenderness in the epigastrium. There was no free acid, but there was persistent occult blood in the stools. X-ray examination showed a fairly large neoplasm in the prepyloric area, which was explored, and was easily movable and resected radically. Her postoperative course was uneventful and she is now living, five years following the operation. She still has what seems to be the initial indigestion, but has maintained her weight and vigor.

Fig. 6.—Case 7., Mr. H.

CASE 6.—Mrs. S., aged 78 years. Accurate history was difficult to obtain due to language difficulties, but for seven months the patient had had marked weight loss, weakness, lack of appetite, and debility. Physical examination showed emaciation and a tumor mass in the left epigastric region which moved on respiration. Gastric

analysis revealed no acid and stools were positive for occult blood. X-ray showed a large neoplastic involvement of the midportion of the stomach with obstruction. Considerable hesitancy was felt about operating on this patient on account of her age and emaciation. However, exploratory laparotomy was done under ether anesthesia and a radical gastric resection performed with ease. No metastases were found. She had an uneventful convalescence and is living and well fourteen months after operation.

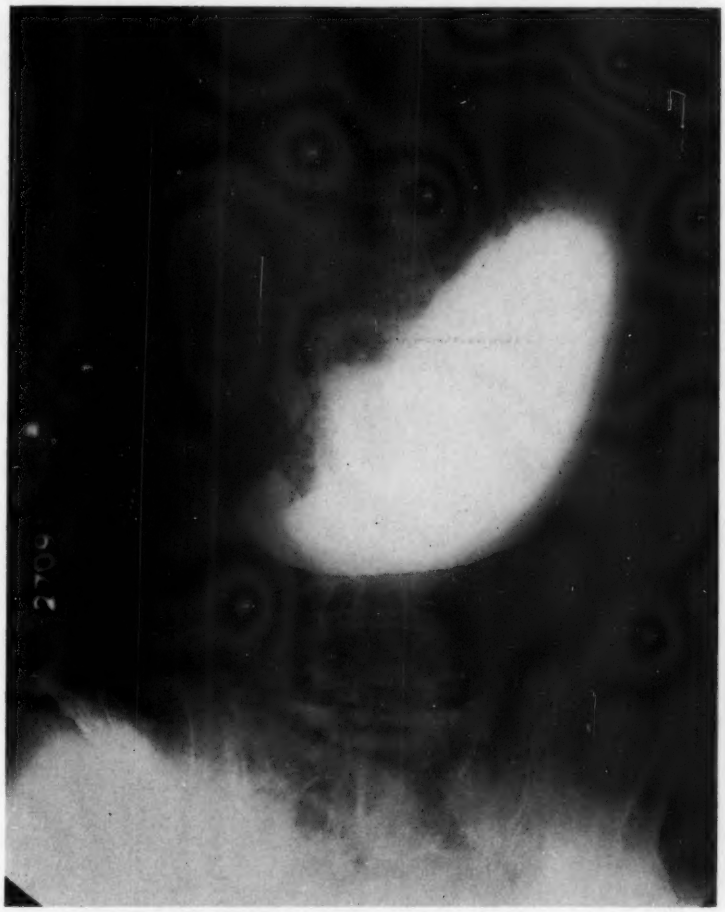

Fig. 7.—Case 8., Mr. C.

CASE 7.—Mr. H., aged 65 years. This patient had a ten months' history of "going downhill." He had mild epigastric pain, a poor appetite, and marked weakness. Examination showed an anemic, emaciated man with a palpable mass in the epigastrium. Gastric analysis revealed no free acid and stools were positive for blood. X-ray showed a large tumor in the prepyloric region and gastroscopy confirmed this. Exploratory laparotomy was done under ether anesthesia and a Hofmeister procedure carried out. The patient had an uneventful recovery with the exception of phlebitis which cleared quickly without special treatment. He is living and well ten months after operation.

CASE 8.—Mr. C., aged 73 years. For one year this patient had been complaining of epigastric pain, and discomfort after eating. He lacked appetite and had lost

weight. Several days before admission to the hospital he began to have fever, chills, and persistent vomiting. Examination revealed a very sick man with a temperature of 39° C. and a picture of an acute condition of the abdomen with rigidity and tenderness in the upper quadrant of the abdomen. With conservative measures the patient recovered from this episode but still continued to run a fever, occasionally vomited, and lost more weight. Gastric analysis revealed no acid and the stools were positive for occult blood. X-ray examination showed extensive neoplastic involvement of almost the entire stomach and gastroscopic report stated that the lesion was hopelessly inoperable. Exploration was done under ether anesthesia, the entire tumor was easily delivered, and a high almost total gastric resection was accomplished. There were no complications and the patient is alive and well, one year and two months following the operation.

Fig. 8.—Case 9., Mrs. MacD.

CASE 9.—Mrs. MacD., aged 82 years. This patient had had indigestion for the past two and one-half years, the underlying suspected condition being gallstones. She was treated by dietary measures for this, but finally she herself began to notice a movable "ball" in the upper abdomen. All this was attended with lack of appetite, loss of weight, and vomiting on occasions. Stool examination was negative for occult blood and the gastric analysis was omitted. The x-ray picture showed a large circumscribed rarified lesion in the region of the pylorus. After a short period of preparation with vitamin therapy and correction of her dehydration, exploration was done under ether anesthesia combined with local infiltration. The en-

tire stomach was easily delivered and a Hofmeister radical gastric resection was performed. The patient was up and out of bed on the third day and ate regular food on the fifth day. Her recovery was entirely uneventful and she is now living and well, nine months after operation.

SUMMARY

From a study of these cases evidence is accumulated which strongly suggests that far from hopeless results may be anticipated in the aged patient with carcinoma of the stomach, and that with prompt recognition of the condition and proper preparation, operation can be safely done with results, if anything, better than in the younger age groups.

TRANSTHORACIC ESOPHAGOGASTROSTOMY

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THE primary object of this report is to comment upon the technical features of an esophagogastrostomy performed upon a patient with carcinoma of the stomach and lower end of the esophagus. The unexpected, successful immediate result demonstrates that this procedure may be used to good advantage for the treatment of esophageal carcinoma that involves any part of the esophagus distal to the bifurcation of the trachea. Transthoracic esophagogastrostomy is now an accepted method of treatment for lesions of the lower third of the esophagus and, although Ochsner and DeBakey,[1] in 1941, collected only seven successful cases, the number now is considerably higher. The operation to be described demonstrates the usefulness of this procedure, also, for lesions of the middle third of the esophagus. Other papers (Carter and Stevenson,[2] Garlock,[3] and Adams and Phemister[4]) may be consulted for a complete review of the treatment of carcinoma of the esophagus.

CASE REPORT.—A white male, 66 years of age, entered the New York Hospital with symptoms of weakness, loss of weight, lower substernal pain of eight months' duration, and vomiting of one week's duration. Physical examination showed a chronically ill man but otherwise was not remarkable. A lesion of the cardiac end of the stomach was demonstrated by x-ray.

Abdominal exploration on June 23 revealed a carcinoma of the posterior wall of the cardiac end of the stomach that extended from the esophageal opening distally for a distance of approximately four inches (see Fig. 1). After satisfactory exposure of the lesion was obtained by mobilizing the upper end of the stomach and dividing the left gastric artery, it was decided that a transthoracic approach would greatly facilitate the removal of the lesion.

Abdominal distention delayed the transthoracic procedure until July 9, sixteen days later. At this time the chest was opened through an intercostal incision in the seventh intercostal space and the seventh to fifth ribs inclusive were divided posteriorly. The lower end of the esophagus was mobilized, following which the diaphragm was opened. It was found that the stomach, spleen, and liver were closely adherent to each other and to the diaphragm, so that it was difficult to establish a line of cleavage. During dissection the splenic vein was injured, which necessitated a splenectomy, but this in turn facilitated the mobilization of the stomach. After division of the vessels along the lesser and greater curvature, the posterior wall of the stomach was removed down to the antrum. From the anterior wall of the stomach a tube, approximately seven inches long, was made and, surprisingly enough, the blood supply appeared to be adequate since the color of the

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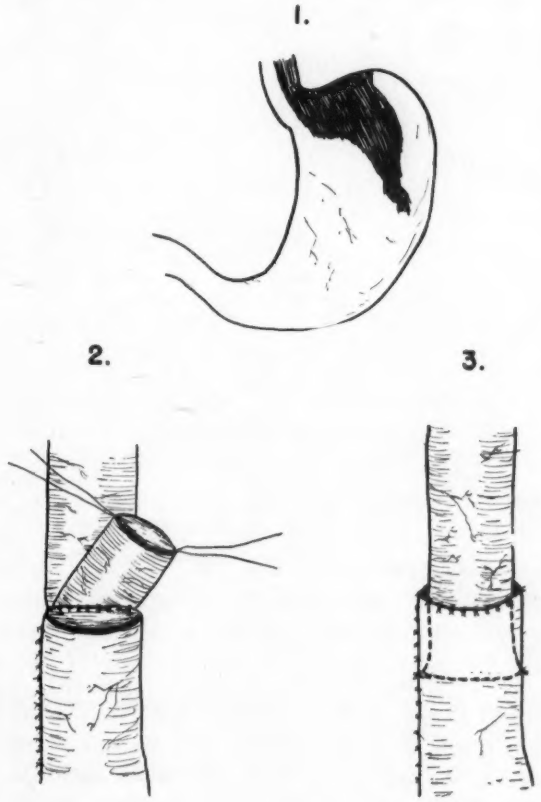
tube remained good. The esophagus was telescoped into the stomach as shown in Fig. 2. The tube of the stomach reached to the aortic arch without difficulty and, consequently, the anastomosis could be carried out without tension. Stay sutures were inserted, anchoring the esophagus to the stomach tube (see Fig. 3) so that the invaginated end of the esophagus would not roll back, as it has been shown to do in dogs.[2] The sutures at the anastomosis approximated the mucosa of the stomach to the muscularis of the esophagus. Finally, omentum was drawn up and sutured snugly about the anastomosis.

The postoperative course was complicated by a localized empyema which responded well to drainage. The patient was discharged six weeks after operation in relatively satisfactory condition and at this time was eating a regular diet. He died about five months after operation from liver metastases. His personal physician reported that until the time of his death he was able to swallow all foods satisfactorily.



The findings and results in this patient bring up several interesting features. The first concerns the importance of performing the transthoracic procedure not more than seven days after the preliminary exploration. In this patient great difficulty was encountered in mobilizing the stomach because of the firm adhesions that had formed within the sixteen days between operations.

On the other hand, in a second patient whose second operation was performed within five days of the preliminary exploration, no technical difficulties were encountered.

CASE REPORT.—A 63-year-old woman complained of dysphagia, loss of weight, and substernal pain of one month's duration. General examination was not remarkable. X-rays revealed a lesion of the cardiac end of the stomach involving the lower third of the esophagus. Preliminary exploratory laparotomy was performed June 9, 1941, and transthoracic esophagogastrostomy by the method described by Garlock with removal of the lower third of the esophagus and cardiac end of the stomach, June 14, 1941. Mobilization of the stomach was accomplished without difficulty. The patient recovered without complication and is well nine months postoperatively.

The question may arise as to whether or not preliminary laparotomy is necessary. Garlock has pointed out the importance of resting this decision upon the results of preoperative biopsy of the lesion. If the lesion is proved to be adenocarcinoma it can be presumed to have arisen either from the stomach or from gastric mucosa situated at the lower end of the esophagus, and these tumors frequently develop early metastases to the liver. However, if the lesion is of the squamous-cell type it probably arises in the esophagus and such tumors metastasize late and involve the liver infrequently. With this in mind, he concludes that whereas for a squamous-cell lesion laparotomy is not indicated, for adenocarcinoma it definitely is. Certainly if x-ray demonstrates that the lesion involves the stomach, a preliminary laparotomy should be done.

The second point of interest is the satisfactory manner in which healing of the anastomosis took place. As detailed, mucosa of the stomach was sutured to muscularis of the esophagus, since it was impossible to invert the stomach so as to approximate serosa to muscularis. At the time this was thought to be most unsatisfactory and, as an additional precaution, the omentum was drawn up into the chest and securely sutured about the line of anastomosis. This, in addition to the telescoping of the esophagus for 2 cm. into the stomach tube, was considered an important feature in the satisfactory healing that took place. In order to confirm this opinion a limited number of experiments were carried out on dogs.

In one group of eight dogs, esophagogastrostomy was performed using a Murphy button to anastomose stomach and esophagus. No omentum was used to reinforce the anastomosis and no sutures were introduced; in this group five of the eight dogs developed a leak at the site of the anastomosis. In a second group of seven dogs, esophagogastrostomy was similarly performed using a Murphy button but, in addition, the omentum was used to envelop the line of sutures. No additional sutures were used. In this group only one of the seven animals developed a leak at the anastomosis.

A third point demonstrated by this patient was the apparent failure of a stricture to form, as evidenced by his ability to swallow solid foods without difficulty. As had been shown by the work of Carter and Stevenson, in animals stricture formation is the usual occurrence follow-

ing an anastomosis in which the esophagus is telescoped for a short distance within the stomach. With this in mind, stay sutures were so placed as to anchor the lower end of the esophagus to the wall of the stomach tube, and it may be that these prevented a stricture (Fig. 3).

Finally, we should like to emphasize the practicability of using transthoracic esophagogastrostomy for all lesions of the esophagus situated distal to the bifurcation of the trachea. Although in this particular patient a tube was made, in many it is possible to bring the entire stomach high into the chest without difficulty and, if the esophagus is sutured without tension, healing has proved, both clinically and experimentally, to take place readily. At any rate, it would seem that this operation may be performed with anticipation of satisfactory results in approximately 50 per cent of the lesions of the esophagus. Whereas in the past a Torek procedure has been considered the method of choice for lesions of the middle third of the esophagus, it would seem that esophagogastrostomy may be used to greater advantage in some cases, not only from the viewpoint of lower mortality but from the viewpoint of the patient's comfort and satisfaction.

REFERENCES

1. Ochsner, A., and DeBakey, M.: J. Thoracic Surg. **10**: 401, 1941.
2. Carter, B. N., and Stevenson, J.: J. Thoracic Surg. **10**: 446, 1941.
3. Garlock, John H.: Surg., Gynec. & Obst. **70**: 556, 1940.
4. Adams, W. E., and Phemister, D.: J. Thoracic Surg. **7**: 621, 1937-1938.

THE TREATMENT OF IMPENETRABLE ESOPHAGEAL STRICTURES BY A COMBINED INTRAESOPHAGEAL AND EXTRAESOPHAGEAL APPROACH

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ESOPHAGEAL obstruction is a rather frequent occurrence. Most of the obstructions are due either to cicatricial stenosis resulting from the ingestion (accidental or suicidal) of strong alkalies or acids, carcinoma of the esophagus, diverticula, or cardiospasm. Less frequently, ulcerations occur from other causes such as peptic ulcer, foreign body, or other inflammatory lesions and result in scarring and stenosis of the esophagus. Carcinoma will not be considered in this discussion.

Complete fusion of the esophageal walls resulting from extensive burns is quite uncommon, but multiple areas of stricture are more frequently seen (Case 3). While there may be complete blocking of the esophagus at one point, usually the remainder escapes such severe injury and can be readily dilated by the usual means. The patient with a complete benign esophageal obstruction presents a difficult therapeutic problem for which many procedures have been advocated and tried, including not only diverse methods of attempting to open and enlarge strictures, but also various attempts to construct an artificial esophagus either intrathoracic or extrathoracic.

Most of the latter have resulted in such poor substitutes indeed for the normally functioning esophagus that it seems advisable to restore the esophagus to its normal function whenever this can be accomplished. This contribution presents a new method of accomplishing this end in the cases not amenable to simple methods.

In the University of Virginia Hospital our records show that a total of fifty-two strictures were encountered in forty-six patients. The site of the strictures varied markedly in relation to the accidental or suicidal ingestion of caustics. In the accidental group approximately 52 per cent were in the upper third, 24 per cent were in the middle third, and 24 per cent were in the lower third. In the attempted suicide group, only 14 per cent were in the upper third, 72 per cent in the middle third and 14 per cent in the lower third (Table I and Fig. 1). Obviously

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the individuals in this suicidal group were not deterred by taste or odor but swallowed the material with determination. Most of the cases of accidental swallowing of strong caustics occurred in children who tend to expectorate promptly anything with an unsatisfactory taste. In the accident group probably a smaller quantity of material was swallowed and the burn did not extend so far down the esophagus.

TABLE I. THE ETIOLOGY AND LOCATION OF THE 52 STRICTURES, ENCOUNTERED IN 46 PATIENTS

CICATRICIAL STENOSIS	UPPER THIRD	MIDDLE THIRD	LOWER THIRD
Lye—accidental	18	8	8
Lye—suicidal	2	10	1
Foreign body—accidental		1	
Ammonia—accidental	1		
Ammonia—suicidal			1
Lime—accidental			1
Acid—accidental	1		
Total—52 cases	22	19	11

Only two patients in our group presented an impenetrable stricture. One of these was in a twelve-year-old colored boy, which followed the accidental ingestion of lye. The other was in an adult who swallowed a large quantity of lye with suicidal intent. This method was also applied in a third case for reasons to be detailed later.

Early Treatment.—If these patients are seen immediately after the ingestion of the caustic, treatment can usually prevent the development of an impermeable stricture. The treatment consists of prompt lavage of the face, mouth, esophagus, and stomach with large quantities of the proper neutralizing solution. A nasal catheter can then be inserted down to the stomach and left in place ten to fourteen days or longer. This may entirely obviate the necessity for a gastrostomy. After three to four weeks the esophagus can be studied by x-ray and any abnormal narrowing noted. If there is any tendency to early stricture, gentle stretching can be done under direct vision through the esophagoscope.

Late Treatment.—Inasmuch as most of the cases do not present themselves for treatment until two to four months after the burn of the esophagus, the problem of stricture continues to present itself. Late cases are forced to seek treatment because of pain and increasing difficulty in swallowing, and usually present marked weight loss. Such patients almost invariably need a gastrostomy, both for feeding purposes and for retrograde bouginage. The gastrostomy should be of such a type, and so placed, that bouginage can be readily accomplished. Gastrostomy of a modified Stamm type in the midportion of the stomach performed in two stages is usually satisfactory. The patient is given a string to swallow and the bougies can then be threaded on the lower end of the string after it is brought out through the gastrostomy opening.

The passage of the string may not be an easy task and may require great skill and ingenuity on the part of the physician.* Many other-

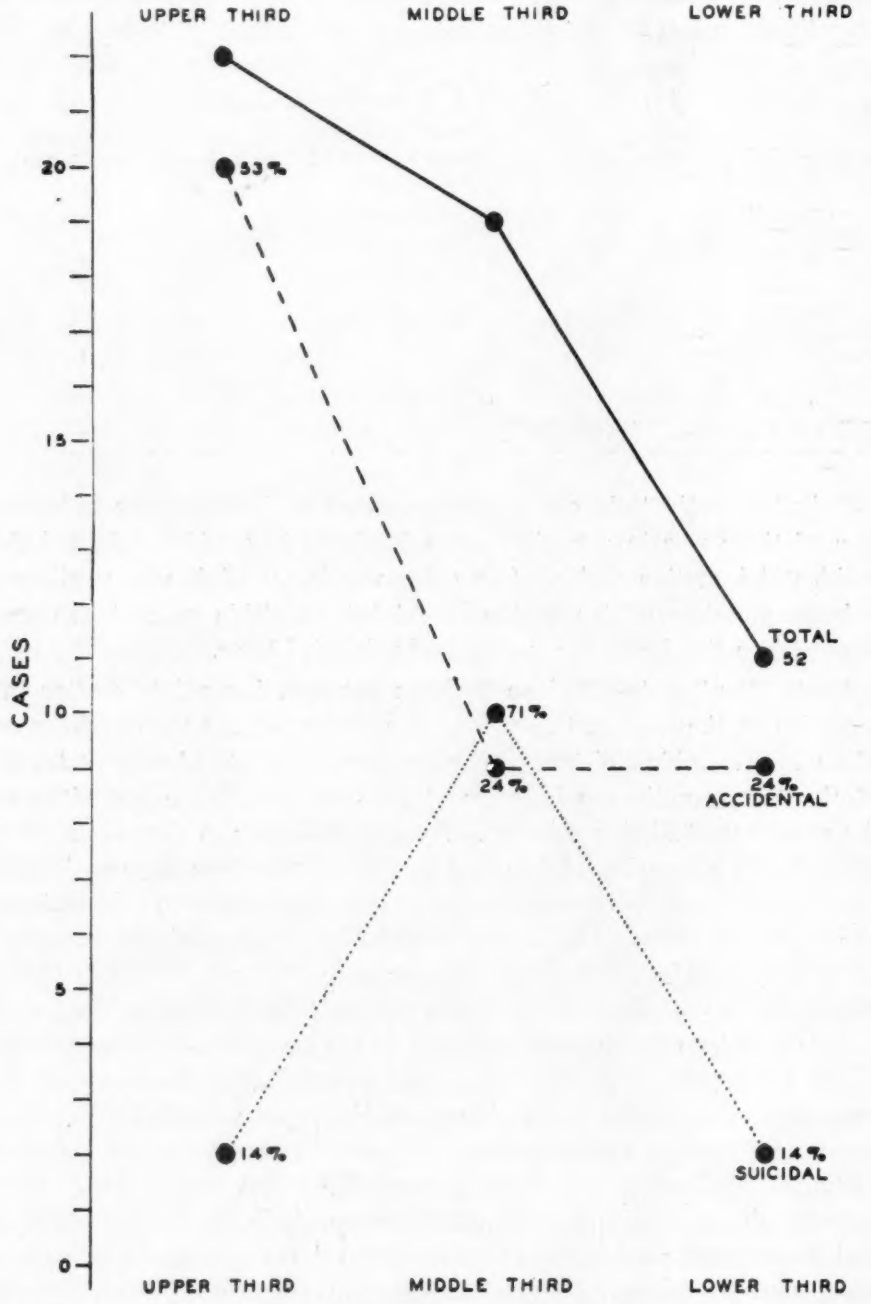

Fig. 1.—A graph showing the location and percentage in each third of the esophagus of the fifty-two strictures.

*The string end bougie dilatations are conducted in the University of Virginia Hospital and outpatient department by the Department of Otolaryngology under the direction of one of us (F. D. W.).

wise impermeable strictures have been successfully treated by the use of the biplane fluoroscope, but not all are amenable to this method.

For a limited group of cases in which these methods have failed on account of complete obstruction of the esophagus, we propose a double approach which has had some measure of success in our hands. It seems worth attempting in the difficult cases rather than to immediately condemn the patient to an artificial esophagus. In simple terms, it consists of guiding bougies through the area of stricture by external

Fig. 2.—Showing the threadlike stricture 2 cm. long in the upper third of the esophagus on admission.

manipulation effected through surgical exposure of the esophagus at the strictured area, but without opening the esophagus. The bougies are passed either from above or below, or both. The method is, of course, more easily applicable in the cervical portion of the esophagus where surgical exposure is simplest, but there is no fundamental reason why it cannot be applied elsewhere in the esophagus. So far we have not had occasion to use the method on a simple stricture of the thoracic portion

of the esophagus although the exposure of the thoracic esophagus in a case of multiple stricture is now planned (Case 3).

The development of this method was the result of several experiences in surgery of the esophagus, in which sharp objects became impaled in the wall of the esophagus so that they could not be removed by means of the esophagoscope alone. We have been able, through external manipulation of the esophagus after surgical exposure, to dislodge them without opening the esophagus. They can then be successfully handled through the esophagoscope. The method also recalls the familiar use of the esophagoscope in the surgical treatment of esophageal diverticulum. The present application of the principle was suggested by one of us (F. D. W.).

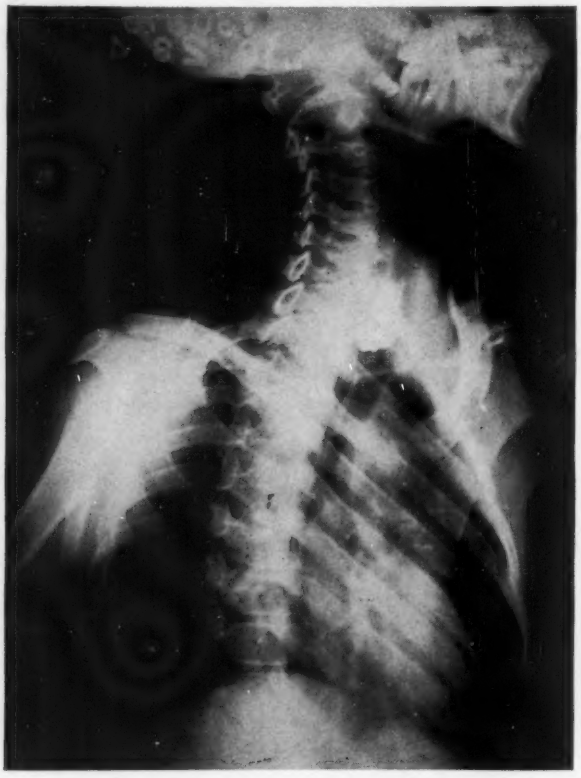

Fig. 3.—Complete stenosis one month later. The esophagus is dilated and atonic above the stricture. Complete stenosis seems to occur more rapidly under gastrostomy feeding and rest of the esophagus.

CASE 1.—(No. 161808.) Lye burn of the cervical esophagus. A 12-year-old negro boy accidentally swallowed lye five weeks before admission. He had been able to swallow nothing but liquids for the preceding two weeks, had lost weight, and had pain and difficulty in swallowing.

X-ray showed a marked stricture 2 cm. long in the upper third of the esophagus (Fig. 2). He was referred to the department of surgery for gastrostomy, which was performed in two stages, five days apart.

The wound was well healed in two weeks and feedings were carried out through the gastrostomy tube. An attempt to have him swallow a string was unsuccessful and it was impossible to pass a ureteral bougie through either the mouth or the gastrostomy. Since the patient was unable to swallow liquids by that time, four weeks after admission, another x-ray examination was made which showed no barium passing the stricture (Figs. 3 and 4). During the next three weeks, repeated attempts to pass a string or bougie from above or below were unsuccessful and it was therefore decided to employ external exposure.

He was operated upon Nov. 16, 1940, approximately seven weeks after admission and twelve weeks after the injury. The operative note is as follows:

Fig. 4.—The radiopaque ureteral bougie is turned back by the complete stricture, when approached from below.

"Under avertin and ether anesthesia an incision was made along the posterior border of the right sternocleidomastoid muscle. Dissection proceeded down to the esophagus, passing laterally and posteriorly to the carotid sheath. The esophagus was identified without difficulty. The esophagus appeared entirely normal to external inspection and examination, but did show some dimpling near the site of the stricture when a bougie was thrust against it. Repeated unsuccessful attempts were made to pass bougies of various materials, tensions, and degrees of sharpness. All important structures were packed off during this manipulation, which was done

slowly and carefully. In spite of every caution, a sharp pointed metal instrument passed through the wall of the esophagus out into the neck on three different occasions. A bougie was then passed through the gastrostomy opening by an assistant. The tip of the bougie which ascended the esophagus could be felt in close proximity to the tip of the bougie which descended from above. At times the two tips seemed to be only a few millimeters apart. It was, however, impossible to permeate the stricture from above or below, while the inferior bougie was in the hands of the assistant. The surgeon, therefore, grasped the esophagus with his left hand and manipulated the bougie from below through the gastrostomy with his right hand. In this way it was possible to guide the lower bougie much more accurately than had been possible previously by giving directions to the assistant. The lower bougie then presented such a clear and well-defined prominence as seen from above through the esophagoscope that it was possible to incise the mucosa overlying the tip of the lower bougie and to allow it to pass freely into the upper esophagus. A string was then tied to the lower bougie and drawn down through the stricture and brought out through the gastrostomy. This entire procedure, guided by the fingers of the left hand of the surgeon, which encircled and manipulated the esophagus from the outside, was carried out with surprising ease considering the long drawn-out and futile attempts that had been made previously. At the conclusion there was no evidence of leakage from the three tiny perforations in the wall of the esophagus. However, sulfanilamide powder was sprinkled freely around the circumference of the esophagus, and a soft rubber drain was brought out at the lower angle of the wound. The incision in the neck was then closed loosely, using interrupted plain zero catgut for the buried sutures and interrupted fine silk for the skin. In spite of the prolonged operation, the boy went through it quite well.''

Retrograde dilatation was started in a few days. The incision in the neck was healed in eleven days. The patient was discharged one month after operation, at which time the stricture had been dilated up to a caliber of 30 French.

Case 2.—(No. 79526.) Spasm of cricopharyngeus muscle (?). A 73-year-old white woman had been having increasing difficulty in swallowing for the past two years. At the time of admission she was only able to swallow liquids, had lost twenty pounds and had frequent attacks of strangling and a sensation of fullness in her chest. Voice weakness and frequent expectoration were also present.

Complete physical examination was negative. Fluoroscopic examination of the esophagus was attempted the day after admission. The barium collected in a small pocket at the level of the upper border of the larynx and none entered the esophagus.

The following day esophagoscopy showed marked obstruction at the upper end of the esophagus. No lumen could be found, but the mucous membranes were normal. Since we suspected that we might have entered a diverticulum, the examination was discontinued and further x-ray studies were ordered.

The next day a lateral x-ray of the neck showed a definite rounded mass 5 mm. in thickness, compressing the posterior aspect of the trachea from the upper level of the larynx downward for 2.5 cm. (Figs. 5 and 6). When barium was swallowed, it stopped as before, but a small trickle entered the esophagus. The roentgenologist reported a tumor in the esophagus, pressing on the trachea.

An attempt to swallow a string the following day was unsuccessful, so a second esophagoscopy was done for the purpose of obtaining a biopsy. Again no mucosa changes were noted and we were unable to enter the esophagus. Several bits of tissue were removed for microscopic examination. The pathologic report showed benign scar tissue with normal overlying epithelium.

Because of this mass of conflicting evidence, we advised external exploration, which was done Aug. 27, 1940. The operative note is as follows:

"Under avertin and novocain anesthesia, an incision was made along the posterior border of the right sternocleidomastoid muscle. The dissection was carried down to the esophagus which was carefully dissected free from the surrounding structures. At no point could any evidence of diverticulum be seen, nor were any other abnormalities evident from an examination of the esophagus on the exterior. At this point the esophagoscope was again inserted in the hypopharynx, and by making traction on the edges of the incision in the neck, the esophagoscope passed easily

Fig. 5.—The mouth and pharynx are filled with barium, but none enters the esophagus.

down into the lower portion of the esophagus. With the esophagoscope in place, a tube was inserted into the stomach. No reason for the obstruction could be determined, either by examining the esophagus from the outside, or by the examination through the esophagoscope on the inside. The patient stood the operation well. The wound was closed loosely, after dusting with sulfanilamide powder, using plain zero catgut for the deeper stitches and silk for the skin, leaving in place a small soft rubber drain at the lower angle of the wound."

She was given sulfanilamide by mouth for five days. Then the stomach tube was removed and soft diet started. She swallowed so well that a regular diet was given three days later which she also took without difficulty. As the neck wound had

healed she was discharged several days later, eating normally, and has had no further trouble.

It is believed that we were dealing with a marked spasm of the cricopharyngeus with perhaps some psychogenic factors in addition. The method employed appears to have been the safest and surest way to relieve her symptoms and to definitely rule out diverticulum and tumor.

Fig. 6.—A lateral view of the neck shows an apparent esophageal tumor, compressing the trachea.

CASE 3.—(No. 83192.) Multiple lye burns of esophagus, upper and lower thirds.

A 27-year-old woman was admitted in June, 1930, with a history of having intentionally swallowed a large amount of lye nine months previously. She was then subsisting entirely on liquids, in small amounts, and had lost considerable weight.

X-ray examination on admission showed a marked stricture high in the upper third and another stricture in the lower third (Fig. 7), and immediate gastrostomy was done. Repeated attempts at permeation both from above and below were unsuccessful, and x-ray two months after admission showed complete occlusion (Fig. 8).

She was sent elsewhere for an attempt at permeation under the biplane fluoroscope. Since this procedure was unsuccessful after repeated attempts, she was sent home to follow a gastrostomy life. She learned to chew her meals and expectorate them into the funnel of her gastrostomy tube; thereby she was able to maintain her nutrition and to carry out the normal obligations of life. Two year later, in 1932, she was again examined, but no opening could be found and she returned home to resume her unhappy existence.

In 1941 she was asked to return to the hospital for a trial of the present method. Although her nutrition was good, she was willing to try anything that offered hope of swallowing in a normal manner. The esophagus was examined by fluoroscopy and the obstruction found to be still complete. Peroral esophagoscopy showed complete obstruction in the upper esophagus. We felt that passing a bougie up from the stomach offered the best chance of permeation, but since we were unable to identify the lower end of the esophagus by retrograde esophagoscopy, it was decided to open the abdominal wall for the purpose of guiding the bougie under finger manipulation. The operative note is as follows:

Fig. 7.—Showing a marked stricture in the upper third of the esophagus, with barium entering the lower esophagus. Fluoroscopic examination showed a second stricture in the lower third, not shown in this film. This was the condition on admission in 1930.

"Under spinal anesthesia a high upper abdominal incision was made and the peritoneum opened. The lower end of the esophagus between the diaphragm and the stomach was found without difficulty, and after numerous attempts, a stiff bougie was finally apparently directed into the esophagus. After this was accomplished, the incision in the abdominal wall was closed in layers, using plain zero catgut for the peritoneum, chrome zero catgut for the superficial fascia, and silk for the skin.

"The patient was then taken to the fluoroscopy room and the bougie examined under the fluoroscope. Unfortunately, it was found that the bougie could not be made to pass farther up the esophagus than the level of the diaphragm. There

seemed to be no doubt that the bougie was actually in the lower end of the esophagus while the operator's hand was inside the peritoneal cavity. The patient went through this lengthy manipulation in good condition.''

The abdominal wound soon healed, so we decided to try permeation from above. After two months at home she returned for this attempt.

Fig. 8.—Complete stenosis two months later. As in Fig. 3, the esophagus is dilated and atonic above the stricture. Again, gastrostomy feeding and rest of the esophagus seem to favor the development of complete stenosis.

On May 9, 1941, the upper esophagus was exposed. The operative note is as follows:

''Under avertin and ether anesthesia, an incision was made along the posterior border of the right sternocleidomastoid muscle. The esophagus was approached by retracting the carotid sheath medially. It was carefully freed from a point above and below the thoracic entrance upward to its junction with the posterior pharynx. Again there was no external evidence in the esophageal wall of the known stricture.

''Various bougies were then passed down the esophagus and manipulated by the fingers of the surgeon in an attempt to guide the instrument down the lumen of the esophagus. After about one hour of manipulation with various types and sizes of instruments, the procedure was abandoned because it was quite impossible to penetrate the stricture. It is felt that had it been possible to pass the bougie upward from below, it might have been possible to penetrate this stricture. At no time was there any evidence of perforation of the esophagus. However, a small amount of

sulfanilamide powder was sprinkled around the circumference of the esophagus and a soft rubber drain was brought out at the lower angle of the wound. The incision in the neck was closed rather loosely, using interrupted plain zero catgut for the buried sutures and interrupted fine silk for the skin.''

The result of these procedures in this patient have failed and she is again leading her gastrostomy life. It should be noted in this case that it was possible to approach each stricture from only one side. The permeation of the stricture is undoubtedly facilitated by approaching it from above and below simultaneously.

DISCUSSION

In two out of three difficult cases of esophageal obstruction which had not yielded to other methods, it was possible through exposure of the esophagus to effect the establishment of a new lumen. In the third case the method failed because of multiple strictures of the organ. In view of the great difficulty attendant upon the treatment of these impermeable cases, it has seemed worth while to present this method of approach.

At the present time it is planned to develop the principle one step further in a final attempt to relieve the patient described in Case 3. Through a transthoracic esophagostomy, bougies will be passed both upward and downward. At the same sitting, attempts will be made to incise the strictures, if possible, through the esophagoscope passed respectively by mouth and by gastrostomy. It is considered safe to open the esophagus under these conditions inasmuch as it has been completely occluded over a period of twelve years. It is possible, of course, that either complete fusion of its wall or additional strictures will be encountered which will, of course, completely prevent the success of this plan of approach. In that event, this patient is an ideal case for the construction of antethoracic esophagus.

CONCLUSION

External exposure of the esophagus is advocated as a safe surgical procedure to aid in the passage of bougies for the permeation of complete esophageal strictures, in selected cases, when other methods have failed.

CARCINOMA OF THE BREAST

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IT IS the feeling of the authors that the radical surgical treatment of cancer of the breast is well standardized. Any further improvement in technique may add to the patient's comfort, but very little improvement in clinical results can be expected from this type of treatment. It is likewise the feeling of the authors that sufficient attention has been paid to the patients who have lived five years or more free of the disease, but that too little emphasis has been given those who fail to survive this period. Often we can profit as much, if not more, from an analysis of our failures. We feel that our five-year end results will not vary markedly from those of other clinics. Consequently, no attempt will be made to review the abundant literature which deals with a purely statistical analysis of five-year survivals. This study, therefore, was undertaken for the purpose of evaluating the various factors which may influence the disease prior to the institution of treatment.

One hundred and ninety-three cases of cancer of the female breast occurring between the years of 1926 and 1936, and followed in our tumor clinic, are the basis of this study. Of this total, 156 patients were subjected to a radical mastectomy in our clinic. Of the remaining thirty-seven patients, fifteen were subjected to a simple mastectomy, ten received radiation only, and in twelve the treatment was done elsewhere and it was impossible to ascertain sufficient data.

TABLE I

DISTRIBUTION OF CASES BY DECADES

DECADE	NUMBER OF CASES	PER CENT
20-30	2	1.0
30-40	14	7.2
40-50	52	26.9
50-60	59	30.6
60-70	48	24.9
70-80	14	7.2
80-90	4	2.0
Total	193	

Table I deals with the distribution of these cases by decades. One hundred and fifty-nine cases, or 83 per cent, occurred in patients between the ages of 40 and 70. Sixteen cases, or 8 per cent, occurred in

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patients under 40 years of age. Eighteen cases, or 9 per cent, occurred in patients past the age of 70. The three decades from 40 to 70 have approximately the same incidence. It is interesting that sixteen patients, or 8 per cent, were under 40 years of age, but as will be shown subsequently, a fair percentage of patients over 40 years of age would have fallen into this group had they sought treatment immediately following the appearance of the first symptom. Therefore, it is important to stress that a routine examination of the female breast in women under the age of 40 is as essential as it is in women above this age. The old adage that any mass in the breast of a woman past 40 years of age be considered malignant leaves one with a false sense of security, and should be revised to state that regardless of the patient's age, a mass in the female breast cannot be considered benign until definitely proved so by histologic evidence.

TABLE II

PREGNANCIES

NUMBER OF PREGNANCIES	NUMBER OF CASES	PER CENT
None	70	36.3
Single	24	12.4
Multiple	99	51.3
Total	193	

Table II deals with pregnancies in relation to the 193 cases of cancer of the breast studied. In seventy cases, or 36 per cent, there were no pregnancies. In twenty-four cases, or 12 per cent, a single pregnancy was recorded. In ninety-nine cases, or 51 per cent, multiple pregnancies occurred. From this small series no deduction can be drawn relative to the influence of gestation on the incidence of cancer in the female breast.

The three primary symptoms were mass in 176 cases, or 91 per cent; pain in thirteen cases, or 7 per cent; and nipple discharge in four cases, or 2 per cent, as seen in Table III. Careful attention should be called

TABLE III

FIRST SYMPTOM

NUMBER OF CASES	MASS		PER CENT		PAIN	PER CENT	NIPPLE DISCHARGE	PER CENT
193	176		91.2		13	6.7	4	2.0
	Discovered by patient	Per cent	Discovered by doctor	Per cent				
	171	97.1	5	2.8				

to the 176 patients who presented themselves with a mass in the breast as their first symptom. One is struck by the fact that in 171 instances the patient was fully aware of the mass in her breast prior to the seeking

of medical advice. Only in five instances was the doctor able to find a mass in the breast without the patient having had previous knowledge of its presence. In a number of instances when the patient presented herself complaining of a "lump" in the breast, the doctor on his first examination was unable to confirm its presence, and it was only after repeated examinations involving a valuable loss of time to the patient that the doctor was able to confirm the presence of such a mass. One cannot overemphasize the fact, therefore, that whenever, a woman presents herself complaining of a lump in the breast, serious consideration should be given to such a complaint. If on the first examination this symptom is not substantiated, it behooves the examiner to make repeated examinations. There are some women who fall into a classification of "hysterical breasts," but this number is comparatively small and one should hesitate to label any woman in this way. As a rule it is not difficult to identify this type of individual. Careful history taking will bring out the fact that the patient is of an unstable, psychogenic personality, and in addition has been overexposed to cancer propaganda.

The second most frequent symptom was pain, and occurred as the first symptom in thirteen cases, or 7 per cent, and was usually of the radiating type. This re-emphasizes the fact that pain is not an early symptom of carcinoma of the breast. Nipple discharge occurred as the primary symptom in only four cases, or 2 per cent. The duration of the first symptom (Table IV) is of interest and probably has some bearing upon the ultimate prognosis of cancer of the breast.

TABLE IV

DURATION OF FIRST SYMPTOM IN 193 CASES

SYMPTOM	NUMBER OF CASES	LESS THAN 3 MONTHS	PER CENT	3 MONTHS TO 1 YEAR	PER CENT	OVER 1 YEAR	PER CENT
Mass	176	64	36.4	40	22.7	72	40.9
Pain	13	8	61.5	0		5	38.5
Nipple discharge	4	2	50.0	1	25.0	1	25.0
Total	193	74	38.3	41	21.2	78	40.4

Sixty-four cases out of 176, or 36.4 per cent, were recorded as having had the lump less than three months. Forty cases, or 22.7 per cent, were recorded as having had the lump three months to one year, and seventy-two cases, or 40.9 per cent, were recorded to have had the lump over one year.

Of the thirteen patients who presented themselves with pain as the initial symptom, eight, or 61.5 per cent, were seen within three months of the onset, and five were seen one year or later after the onset. Of the four patients who complained of discharge from the nipple as the first symptom, two were seen within three months, one within six months,

and one within two years. It is interesting to note that of the seventy-four patients seen within three months after the recorded onset of symptoms, twenty-four, or 32 per cent, were found to have histologic involvement of the axillary nodes. It seems more probable that the initial symptom in these twenty-four cases was of a longer duration.

In view of the afore-mentioned, a study was made to determine the five-year end result in relation to the duration of the first symptoms (Table V). Of the seventy-four patients with a duration of the present-

TABLE V

FIVE-YEAR END RESULT IN RELATION TO THE DURATION OF THE FIRST SYMPTOM

DURATION OF PRESENTING SYMPTOM	NUMBER OF CASES	NUMBER OF PATIENTS ALIVE AND WELL 5 YEARS LATER	PERCENTAGE WELL 5 YEARS LATER
Less than 3 months	74	30	40.5
3 months to 1 year	41	13	31.7
Over 1 year	78	16	20.5
Total	193	59	30.6

ing symptom less than three months, thirty, or 40.5 per cent, were alive and well five years later; of the forty-one patients with the duration of the presenting symptom three months to one year, thirteen, or 31.7 per cent, were alive and well five years later; and of the seventy-eight patients with the presenting symptom of one year or longer, sixteen, or 20.5 per cent, were alive and well five years later. Of the total of 193 cases, 59, or 30.6 per cent of the patients were alive and well five years later. On the basis of these findings, it would seem that the best results are obtained in those patients with the shortest positive history, and as the time interval between the initial symptom and the seeking of medical advice is increased, the prognosis for a five-year arrest of the disease is reduced.

TABLE VI

QUADRANT LOCATION OF TUMOR

QUADRANT	NUMBER OF CASES	PER CENT
Outer half	122	63.2
Inner half	31	16.1
Center	32	16.6
Not obtainable	8	4.1
Total	193	

The location of the tumor by quadrant is represented in Table VI. One hundred and twenty-two cases, or 63 per cent, occurred in the outer half; thirty-one, or sixteen per cent, in the inner half; and thirty-two, or 16 per cent, in the central portion of the breast. In eight cases the location of the mass was not recorded. In Table VIII an analysis of the end results by quadrant location is recorded in the 156 cases in which the

patients were subjected to radical mastectomy. Table VII is included to indicate the type of treatment accorded the 193 cases.

TABLE VII

CLASSIFICATION ACCORDING TO TREATMENT

TYPE OF TREATMENT	NUMBER OF CASES	PER CENT
Radical mastectomy	156	80.8
Simple mastectomy	15	7.8
Radiation only	10	5.2
Insufficient data	12	6.2
Total	193	

The end results in the 156 patients subjected to a radical mastectomy were studied from the standpoint of the location of the primary tumor with and without proved axillary metastases. Of the total of the eighty-six cases involving proved axillary metastases, the primary tumor was located in the outer half of the breast in fifty-six patients. Twenty, or 35.7 per cent, were alive and well at the end of five years. In twelve instances the primary tumor was in the inner half of the breast, and only one, or 8.3 per cent, was alive and well at the end of five years. Of the eighteen patients with the tumor located in the center of the breast, three, or 16.6 per cent, were alive and well after five years. Twenty-four patients, or 27.9 per cent, represent the five-year survivals in the group of eighty-six with proved axillary metastases. Seventy cases without axillary metastases were studied from a survival viewpoint. Forty-three occurred in the outer half, and twenty-three patients, or 53.4 per cent, were alive and well five years later. Thirteen occurred in the inner half, and six patients, or 46.1 per cent, were alive and well five years later. Fourteen occurred in the center of the breast, and six patients, or 43 per cent, were alive and well five years later. Of the total of seventy cases, thirty-five patients, or 50 per cent, were alive and well five years later, as seen in Table VIII.

TABLE VIII

156 CASES OF RADICAL MASTECTOMY

END RESULTS

LOCATION OF PRIMARY TUMOR	WITH PROVED AXILLARY METASTASES			WITHOUT AXILLARY METASTASES		
	NUMBER OF CASES	NUMBER OF 5-YEAR SURVIVALS	PER CENT OF 5-YEAR SURVIVALS	NUMBER OF CASES	NUMBER OF 5-YEAR SURVIVALS	PER CENT OF 5-YEAR SURVIVALS
Outer half breast	56	20	35.7	43	23	53.4
Inner half breast	12	1	8.3	13	6	46.1
Center of breast	18	3	16.6	14	6	43.0
Total cases	86	24	27.9	70	35	50.0

It would seem from Table VIII that the best chance for a five-year survival is in the patient who has a tumor in the outer half of the breast.

This is especially so in those cases without axillary metastases. The worst prognosis seems to be in those patients with proved axillary metastases in which the primary tumor was located either in the inner half or the center of the breast.

Aside from the disease itself, elephantiasis has been one of the most troublesome complications. Two hundred and ninety-eight cases followed between the years of 1926 and 1941 were studied from this standpoint (Table IX). Of this total, ninety patients, or 30.2 per cent, developed elephantiasis following radical mastectomy. We did not consider any case as being satisfactory for this group unless there was a persistent increase in the circumference of the affected arm one inch more than that of the contralateral side. No attempt was made to evaluate the patient on a functional basis of the arm. It was felt that the cases should be studied to determine if the involvement of the axillary glands was a factor in the incidence of elephantiasis. In 167 cases, or 56.3 per cent, such involvement was shown. We could find no appreciable difference in the incidence of the elephantiasis between the group showing positive axillary nodes and the group which did not.

TABLE IX

ANALYSIS OF ELEPHANTIASIS IN 298 CASES
(1926-1941)

		PER CENT
Total number of cases	298	
With elephantiasis	90	30.2
Without elephantiasis	208	69.8
Total number with positive nodes	167	56.3
With elephantiasis	55	32.9
Without elephantiasis	112	67.1
Total number with negative nodes	131	43.7
With elephantiasis	35	26.7
Without elephantiasis	96	73.3

Further analysis reveals that in forty-nine cases involving radical mastectomy, the operation was supplemented by a skin graft procedure

TABLE X

ANALYSIS OF ELEPHANTIASIS IN 49 CASES WITH SKIN GRAFT

		PER CENT
Total number with skin graft	49	
With elephantiasis	10	20.4
Without elephantiasis	39	79.6
Total number with positive nodes	28	57.1
With elephantiasis	6	21.4
Without elephantiasis	22	78.6
Total number with negative nodes	21	42.9
With elephantiasis	4	19.0
Without elephantiasis	17	81.0

(Table X). Ten patients, or 20.4 per cent, developed elephantiasis. Here again there is very little appreciable difference, in the incidence of elephantiasis, between the group of patients having axillary involvement and the group without. However, there was a consistent reduction in the incidence of elephantiasis of approximately 10 per cent in those patients having the added benefit of a skin graft over those cases who did not.

DISCUSSION

One hundred and ninety-three cases of cancer of the breast have been studied to determine what factors other than treatment may influence the clinical results. Likewise, 298 cases of cancer of the breast were studied to determine the effect of skin grafting upon the incidence of elephantiasis.

From these studies it would appear that cancer of the breast occurs much more frequently in women under 40 years of age than is generally appreciated. Likewise, it has been shown that the patient is in a position to recognize the early symptoms and signs which indicate abnormalities of the breast. Furthermore, it was found that the percentage of five-year survivals was highest in those patients with the initial symptom of less than three months' duration. The five-year survival in this group is 40.5 per cent. With the increase in the duration of the presenting symptom from three months to one year, 31.7 per cent were alive, and in the group over one year the percentage had dropped to 20 per cent. From these findings it would seem that there is room in the field of preventive medicine on the part of the practitioner to stress to his patient the importance of seeking medical advice as soon as the abnormality is noted. When the tumor is located in the outer half of the breast the chance of a five-year survival was greater than in any other location. When the tumor was not in the outer half, and it was found at operation that the axillary nodes were involved, the prognosis for a five-year survival was extremely poor.

From the study of 298 cases relative to elephantiasis, it was found that a skin graft was of definite value in decreasing the incidence of elephantiasis. Although the difference is not striking in our series, we are certain that there would have been a greater disproportion if the skin graft had been more complete. Halsted stressed the importance of leaving the wound open and placing the grafts high in the axilla to avoid tension and contracture. In some of our cases it was apparent from the operative note that the skin grafting failed to accomplish this. If the graft is not placed in the apex of the axilla, it fails to accomplish the purpose of obliteration of the dead space. We have observed local recurrences in a number of the skin grafts, and it is our feeling that skin grafting plays a very little part in decreasing the incidence of such recurrences.

CONCLUSIONS

1. Clinical end results in cancer of the breast seem to bear a relationship to the duration of the initial symptom.

2. Too long an interval exists between the patient's awareness of the initial symptom and the institution of treatment.

3. Skin grafting is a definite factor in the reduction of the incidence of elephantiasis.

4. Skin grafting is no assurance against local recurrences.

5. Skin graft should be placed in the apex of the axilla. Otherwise it does not fulfill its function of doing away with the dead space.

WHIPPLE'S DISEASE, OR INTESTINAL LIPODYSTROPHY

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WHIPPLE, in 1907, described a disease which was "characterized anatomically by deposits of fat and fatty acids in the intestinal and mesenteric lymphatic tissues," and which he termed *intestinal lipodystrophy*. This disorder caused loss of weight to the point of emaciation; loss of strength; microcytic anemia; recurrent arthritis; doughy swelling of the abdomen associated with tenderness and gaseous distention; and fatty diarrhea with an average of three or four stools a day, which were light or clay colored and consisted of over 50 per cent fat and fatty acids, by weight. There was no interference with fat splitting for the fat in the stool was almost completely composed of split fats and soaps in crystalline form.

Blumgart reported three cases of malabsorption of fat "which were not in accord with any hitherto recognized diagnosis, and which, because of similar signs, symptoms, course and postmortem findings, strongly suggested a definite disease entity." He states, "It would seem that a definite clinical and pathological syndrome with such an intangible etiologic background must have been previously recognized. Nevertheless, search of the literature has uncovered only one analogous case, reported by G. H. Whipple."

In 1936, Jarco reported a case of steatorrhea with unusual intestinal lesions which he felt had "great clinical similarity and virtual anatomical identity" with that described by Whipple.

The most recent description of this condition is by Reinhart and Wilson, who report a case of malabsorption of fat that was considered to be identical with those mentioned above. They compared the histologic slides of this case with those of Whipple and Jarco and felt that "the anatomical lesions were of the same basic type."

The case herein reported is considered to be of this group and is the seventh case described. It is the first in which the diagnosis was made during life, which permitted metabolic studies and observations on the effect of treatment. The true nature of the condition in this case was not established until Whipple examined the material removed at operation and made the diagnosis.

REPORT OF CASE

H. B. (No. 158533, S. M. H), a 59-year-old farmer, dates his present illness to fifteen years ago when he began having attacks of right upper quadrant abdominal

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pain of a colic-like nature associated with nausea, vomiting, and jaundice. The pain occasionally radiated to the right shoulder, was aggravated by fatty food, and was relieved by bed rest. These attacks have not varied in frequency or severity in the intervening years but have continued more or less independently of his other complaints.

Thirteen years ago he began having pain, stiffness, and limitation of motion of the joints, particularly of the hands and knees. These arthritic symptoms were severe for eight years and subsided somewhat after the extraction of his teeth.

For the past two years he has had recurrent bouts of abdominal distention, associated with an intermittent crampy pain, and with diffuse tenderness of the abdomen. At times he has vomited large amounts of green fluid and at other times has retained ordinary food though his intake has been below normal. These recurrent attacks of abdominal pain and distention became so numerous and so severe that he was admitted to the Batavia Hospital in March, 1939, where a partial obstruction of the sigmoid colon was found. The symptoms of pain, vomiting, and abdominal distention became worse and he was operated upon June 3, 1939, at which time release of adhesions and a biopsy were done. The pathologic report of the tissue removed was "chronic inflammation."

Since there was little or no improvement after this operation, he was referred here on Oct. 20, 1939. Examination showed a chronically ill, white male of 59 years of age, who had pallor of the oral mucous membrane, no teeth, a lemon yellow tint to the skin, and no glandular enlargement. The lungs were clear, the right diaphragm was a little high, and the heart was enlarged to the left with a soft systolic apical murmur. The cardiac rhythm was fundamentally regular but ventricular extra systolies were occasionally present. There was peripheral arteriosclerosis with a blood pressure of 128/80 mm. Hg. The extremities showed arthritic changes but no edema.

Examination of the abdomen revealed marked gaseous distention associated with generalized tenderness most marked in the left lower quadrant. The abdomen had a peculiar consistency best described as "doughy," for resistance was felt without the presence of muscle spasm. No free fluid could be demonstrated. It was thought that multiple masses were present but they could not be certainly defined because of the gaseous distention. When x-ray examination showed partial intestinal obstruction, operation was advised and done on Oct. 23, 1939.

When the abdomen was opened it was found that all the viscera were matted together in one solid mass. After adhesions were freed the loops of the intestine were seen to be bound together by a gelatinous appearing substance which, when released, was found to be a clear fluid. The intestinal loops were red, granular, and covered with a shaggy exudate. There were hard, pale pink nodules in the liver and on the intestines, omentum, and parietal peritoneum. This picture was unlike pseudomyxoma peritonaei or colloid carcinomatosis in that the colloid appearing substance became fluid on its release and the nodules when cut were found to be hollow cysts containing a yellow oily substance. Several of these nodules were removed for histologic examination, many adhesions were released and the abdomen closed.

The patient made an uneventful convalescence from this operation. The report on the tissue removed states that many large phagocytic cells with foamy cytoplasm and many giant cells were present in a connective tissue stroma surrounding cystic areas. Special stains showed these foam cells and giant cells to be loaded with fat droplets. When the sections were shown to Dr. G. H. Whipple, he made the diagnosis of intestinal lipodystrophy and stated that the lesions were the same as those he had described previously. This authoritative confirmation of the diagnosis gave confidence in proceeding with laboratory and metabolic studies, for this case was unique in that the diagnosis had been made during life.

The patient was discharged on a low fat diet and bile salts (sodium taurocholate 0.5 Gm. three times daily). Soon after his discharge from the hospital he began having abdominal pain which originated in the right upper quadrant and radiated

TABLE I

LABORATORY FINDINGS

Urine

Albumin	0
Sugar	0
Mic.	Negative

Blood

W.B.C.	7,700-9,100
Hb.	11.0-12.5-14 Gm.
R.B.C.	4,030,000-4,730,000
Differential	
Neutrophiles	85%
Lymphocytes	12%
Eosinophiles	2%
Monocytes	1%
Smear	
Few microcytic	R.B.C.
Reticulocytes	1.4%
Blood group	A
Wassermann	Negative

Glucose Tolerance Test

	11/13/39	3/13/41
Fasting	72 mg. %	86 mg. %
½ hour	114 mg. %	135 mg. %
1 hour	123 mg. %	143 mg. %
1½ hour	127 mg. %	--
2 hour	87 mg. %	102 mg. %
3 hour	62 mg. %	71 mg. %

Blood Chemistry

Chlorides	585-595
N.P.N.	25- 35
Icterus index	6
CO_2 comb. P.	50%
Amylase	80-140
Serum albumin	4.25
Serum globulin	1.65
Total protein	5.90-6.8
Calcium	9.1
Phosphorus	4
Phosphatase	3.2 (Bodansky units)

Blood Fats

	Phospholipid	Cholesterol	Total
No. 1	268	152	769
No. 2	310	173	959

Fluid in Intra-abdominal Nodules

Fatty acids	74%
Cholesterol	12.5%
Phospolipid	2.06%

through to the back in the intrascapular region. This persisted and he was readmitted to the hospital two months after his discharge. The findings led to a

TABLE II

Vitamin A Absorption—7000 I.U. Vitamin A per Kilogram

BEFORE TREATMENT (11/5/39)		AFTER TREATMENT—BILE SALTS (3/13/41)
Fasting	30	39 units per 100 c.c.
2 hours		39 units per 100 c.c.
4 hours		36 units per 100 c.c.
6 hours	108	110 units per 100 c.c.
8 hours		548 units per 100 c.c.
12 hours	291	402 units per 100 c.c.
Carotene	14	50 units per 100 c.c.
Xanthophyll	25	77 units per 100 c.c.

Metabolic Studies After Bile Salts—Diet Contains 100 Gm. Fatty Acid

	STOOL	
	BEFORE TREATMENT (11/2/39)	AFTER BILE SALTS (3/13/41)
	Pale, creamy, foul, guaiac negative	Brown, formed, guaiac negative
Lipid-dry stool	59.5%	25%
Split fat	44.2%	20%
Neutral fat	12.2%	
Unsaponifiable	3.1%	5%

diagnosis of cholecystitis, which was confirmed by intravenous cholecystogram, but because of his poor condition operation was deferred and he was discharged. He returned one month later, stating that the attacks of pain had become more frequent and severe and were now associated with profuse vomiting. It was thought possible that the cholecystitis was a factor influencing the lipodystrophy; cholecystectomy was advised.

Operation was done Jan. 4, 1940, at which time the right upper quadrant of the abdomen was freed of the adhesions that had prevented its inspection at the previous laparotomy. Large masses of the cystic nodules were on the under surface

Fig. 1.—The appearance of the abdominal viscera in Whipple's disease, as seen at the second operation. Many adhesions were freed before this view was obtained. In the insert, one of the nodules is cut to show its hollow center.

of the liver on either side of the gall bladder (Fig. 1). Several of these were removed and the gall bladder was excised. He recovered satisfactorily from this operation and was sent home on a low fat diet, sodium taurocholate, calcium, and vitamin A. He improved remarkably, gained weight and strength, and was able to return to work. One year later he was readmitted to the hospital for metabolic studies consisting of vitamin A and fat absorption tests on a diet containing 100 Gm. of fatty acid. The results are shown in Table II, where it will be seen that in comparison to the data of November, 1939, there is a great improvement in the absorption of fat. This was obtained after prolonged, continuous administration of bile salts and it was decided to discontinue this medication to determine the result. Shortly after this, symptoms of indigestion, nausea, gas, and diarrhea

occurred. Bile salts were resumed and the symptoms disappeared. This was tried a second time with the same result, therefore the patient was instructed to continue indefinitely on bile salt medication. He is now well.

DISCUSSION

The pathologic changes in intestinal lipodystrophy as originally given by Whipple may well be repeated here, for nothing can be added to that description. He says: "The villi of the small intestine are enlarged by deposits of osmic acid reducing bodies (neutral fats and fatty acids). Such deposits are most numerous in the glands, but alike in all these situations. They are of all sizes from minute grains, intra- or extracellular in location, up to huge irregular droplets and there is the greatest variety of forms. Many of the larger masses show rosettes of fatty acid crystals and they may occupy spaces which are lined by endothelium suggesting dilated lymph channels. The majority of the larger deposits are outlined by polynuclear giant cells or large mononuclear cells of polyblastic type which in some instances seem to be eroding the fatty material and are closely applied to its edge. The epithelium of the *mucosa* is normal as far as the microscope shows. The interglandular stroma contains about the usual number of lymphocytes, plasma cells, and eosinophiles, but there is an infiltration with great numbers of polyblasts—large mononuclear, ameboid cells with pink granular protoplasm. A second type of cell which is very conspicuous has an abundant foamy protoplasm, a pale vesicular nucleus and is actively ameboid; this may be a type of polyblast. Ecchymoses are numerous wherever we find the fatty deposits. The submucosa shows invasion with great numbers of these polyblastic cells especially about the fat deposits which in some places are abundant, in others absent. There may be a very definite eosinophilia in such areas. The *glands* show the most extensive changes, especially the larger ones. In some the lymphatic nodules and cords are quite intact, the process seeming to begin in the sinuses of the glands with invasion of the characteristic cells and small irregular fat deposits. The next stage is an invasion by fibroblasts and capillaries with more or less extravasation of blood, increase in size and number of the fat deposits and distortion of the gland architecture. The large mononuclear cells increase rapidly in numbers and giant cells become conspicuous. The final stage shows a very large gland packed with fat deposits of all sizes and shapes, whose stroma is made up of dense fibrous tissue full of ecchymoses and great numbers of giant and mononuclear cells."

The oily substance in the cystic nodules was found to be 74 per cent fatty acid (Table II). It is probable that this nodular lesion results from a protective fibroplastic reaction around fat that is liberated within the peritoneal cavity.

The response of this patient to bile salt administration suggests that the disorder may be due to a fault in bile salt metabolism. Unfortunately, quantitative tests are not available to determine the level of bile

salts in the blood so an analytical study of their metabolism is not possible. When bile salts are given in adequate dosage the patient's symptoms disappear, vitamin A absorption improves, and the fat content of the stool approaches normal. The symptoms return if bile salt administration is stopped and are relieved with resumption of treatment. Another significant fact is that much of the fat is split into fatty acids so that the fault present in the disease is apparently connected with abnormal absorption and utilization of fat.

These facts point to a disturbance of bile, particularly the bile salt metabolism which appears to be deficient. Whether this lack is caused by a faulty production or by abnormal loss of the bile salts cannot be determined, nor can it be proved by analytic studies that this hypothesis of the etiology is correct. But for the present, at least, this concept gives a satisfactory working basis for the management of the disease.

SUMMARY

1. Whipple's disease or intestinal lipodystrophy is characterized by deposits of fat and fatty acids in the intestinal and mesenteric lymphatic tissues, the matting together of the abdominal viscera, and the formation of hard nodules containing lipids in the liver and on all of the peritoneal surfaces.

2. The disease causes loss of weight to the point of emaciation, loss of strength, microcytic anemia, recurrent arthritis, doughy swelling of the abdomen associated with tenderness and gaseous distention, and fatty diarrhea.

3. The disorder is important surgically because it may be confused with gall bladder disease, intestinal obstruction, or carcinomatosis. The latter condition is suggested by the finding of a colloid-appearing substance and the presence of hard, pale pink nodules which resemble the lesions of metastatic carcinoma. Thus, a hopeless prognosis may be given whereas actually the outlook is favorable with adequate treatment.

4. Analytic data are presented which suggest that the abnormal fat digestion present in the disease is due to a fault in bile salt metabolism. This view is strengthened by the clinical response to bile salt administration but it cannot be proved until suitable analytic methods are available.

I am indebted to Dr. S. H. Bassett, Dr. W. R. Bloor, and Dr. A. B. McCoord for their cooperation in making the analytical chemical studies.

REFERENCES

1. Whipple, G. H.: A Hitherto Undescribed Disease Characterized Anatomically by Deposits of Fat and Fatty Acids in the Intestinal and Mesenteric Lymphatic Tissue, Bull. Johns Hopkins Hosp. **18**: 382, 1907.
2. Blumgart, H. L.: Three Fatal Adult Cases of Malabsorption of Fat, Arch. Int. Med. **32**: 113, 1923.
3. Jarco, Saul: Steatorrhea With Unusual Intestinal Lesions, Bull. Johns Hopkins Hosp. **59**: 275, 1936.
4. Reinhart, H. L., and Wilson, S. J.: Malabsorption of Fat (Intestinal Lipodystrophy of Whipple), Am. J. Path. **15**: 483, 1939.
5. Sailer, S., and McGann, R. J.: Lipophagic Granulomatosis of the Enteric Tract Am. J. Digest. Dis. **9**: 55, 1942.

SURGICAL TREATMENT OF SPASMODIC FACIAL TIC

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VERY little concerning facial spasm has been written in the American literature during the past five years. Two significant papers on the subject appeared in 1937. Howe, Tower, and Duel[2] reported the appearance of fibrillary motor overflow in the muscles of the face after facial nerve regeneration following nerve section in monkeys. They ascribed this to axonal branching during nerve regeneration. This type of fibrillary motor overflow is seen, not infrequently, after recovery from Bell's palsy.

Coleman[1] was able to obtain satisfactory relief of severe tonic and clonic facial spasm, at the cost of partial facial paralysis, by section and resuture of primary facial nerve branches. Recurrent spasm appeared in six to twelve months. More lasting relief was obtained by complete section of the facial nerve, with hypoglossal anastomosis. The results of hypoglossal anastomoses are not ideal but are preferable to complete facial paralysis. Temporary relief of facial spasm was also obtained by alcohol injection of the facial nerve at the stylomastoid foramen, again at the cost of facial paralysis.

Facial spasm may be tonic in type, sometimes a sequela of encephalitis. More common is the clonic type; idiopathic, paroxysmal spasms, provoked by eating, talking, smoking, or emotional tension. It is more common in women, middle-aged to elderly. The muscles most frequently involved are the orbicularis oculi, the xygomaticus, and risorius, but minor or major spread to the other facial muscles, even the platysma, is common. The spasm is occasionally bilateral. The incidence of facial spasm is much less than that of trigeminal neuralgia, and somewhat greater than that of glossopharyngeal neuralgia.

The therapeutic objective is obvious: relief of spasm without paralysis of the face. So far this has not been attained. In some respects the problem is similar to that of trigeminal neuralgia. It is a common experience in this latter condition that incomplete root section or alcohol injection may be followed by satisfactory relief of pain without complete loss of sensation in the involved area. It appeared possible that a similar situation might obtain in the case of the facial nerve. The present operation was designed on this basis.

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The surgical procedure, done under local anesthesia, is carried out through a vertical incision just anterior to the ear. The dissection is directed anteriorly along the parotid fascia to the anterior border of the parotid gland (Fig. 1), and the primary branches of the facial nerve are identified at this point. The several primary branches are then stimulated electrically, with the face sufficiently exposed to identify the functional destination of each branch. Those branches which, upon stimulation, cause contraction of those muscles especially involved in the facial

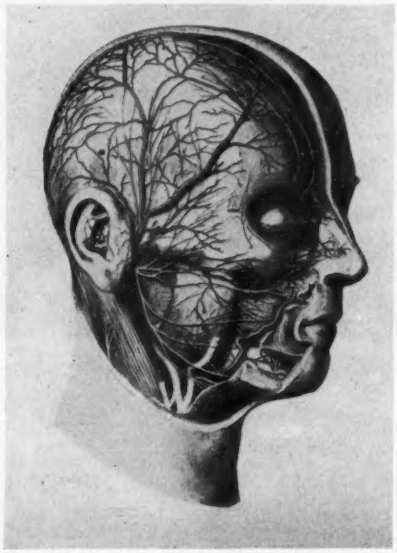

Fig. 1.—Anatomic relations of the facial nerve. The parotid gland has been divided to demonstrate the primary branches of the nerve.

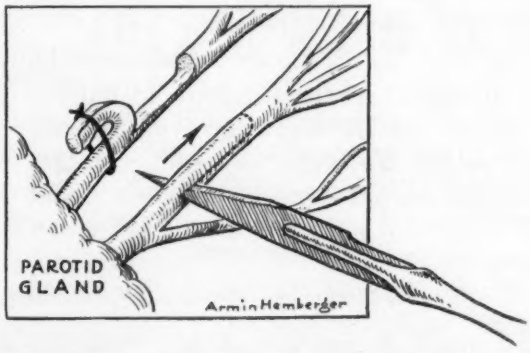

Fig. 2.—Diagrammatic sketch of operation. Note loose ligature holding nerve flap in reverse direction.

spasm are isolated preparatory to partial section. In the earlier cases the appropriate branches were simply divided through about three-quarters of their diameter. In the more recent cases (Fig. 2) a small nerve flap was made, composed of three-quarters or more of each in-

volved branch, and the free proximal segment held loosely in a reversed direction by a lightly tied suture.

Four patients have been operated upon in this manner. The follow-up is incomplete on one patient because of his death, presumably from

Fig. 3.—Photograph of patient, one month after nerve flap operation on right facial nerve.

coronary thrombosis, at a considerable interval after discharge from the hospital; satisfactory relief without paralysis had been obtained up to that time. The operation was repeated on two occasions, at intervals of a year in one case. Satisfactory relief without paralysis was attained after each of the three operations. The last two patients were operated upon within the past year and it is too soon to judge the duration of relief. With the exception of slight temporary weakness of the face immediately after operation, there was very little evidence of motor impairment (Fig. 3). At times, on spontaneous blinking, there appeared to be a slight lag of the involved lid but this was hardly detectable. It is hoped that the nerve flap type of section used in the last two cases may prolong the period of relief. In any case, it is quite feasible to repeat the operation when the spasm recurs.

REFERENCES

1. Coleman, C. C.: Surgical Treatment of Facial Spasm, Ann. Surg. **105**: 647, 1937.
2. Howe, H. A., Tower, S. S., and Duel, A. B.: Facial Tic in Relation to Injury of the Facial Nerve, Arch. Neurol. & Psychiat. **38**: 1190, 1937.

OBSERVATIONS AND SURGICAL ASPECTS OF THE CAROTID SINUS REFLEX IN MAN

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THE carotid sinus reflex began to assume importance as a factor in the control of vasomotor and other autonomic effects with the experimental work in animals by Hering (1927[6]), de Castro (1928[2]), and Heymans (1929[7]). To Weiss and his co-workers goes much of the credit for bringing to wide attention the significance of the carotid sinus reflex, particularly in its abnormal phases, in man. In 1933 Weiss and Baker[17] presented evidence to show that the abnormal state of the carotid sinus reflex may be responsible for certain symptoms, the most spectacular of which is syncope. Increasing evidence of the existence of what has come to be known as the "carotid sinus syndrome" has now been reported by numerous observers.[4, 5, 10, 11, 13, 18] It has developed that the carotid sinus is but one of many components on the afferent side in the reflex maintenance of the tonus of the autonomic nervous system. Because of this fact there has been misgiving on the part of some in accepting unqualifiedly the carotid sinus syndrome as a manifestation of hypersensitivity of the carotid sinus alone. Our experiences with the carotid sinus reflex in a selected group of surgical cases may serve to add to the accumulating information in this field of inquiry.

A brief review of the significant aspects of the carotid sinus reflex will serve to summarize the subject. Elsewhere the details may be found in monographs.[5, 17]

The carotid sinus may be thought of as comprising the bulbous dilatation of the first portion of the internal carotid artery and perhaps small contiguous portions of the external and common carotids. Its walls are supplied by a dense plexus of nerves lying in the "Y" of the bifurcation of the common carotid (Fig. 1). This plexus connects by way of the "carotid sinus nerve" (nerve of Hering) with the ninth cranial (glossopharyngeal) nerve and also with the tenth (vagus) and twelfth (hypoglossal) cranial nerves and the cervical sympathetics.[15] Certain of the receptor endings appear to respond to stretch or pressure and others to chemical stimuli.[8] Impulses which arise in the carotid sinus pass centrally to stimulate numerous autonomic centers. Constant stimuli from the carotid sinus exert a tonic inhibitory effect on the

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vasomotor centers and when the afferent impulses subside these centers overreact, at least until compensated for by the numerous other afferent mechanisms. Thus, changing arterial pressure within the carotid sinus brings about a fall in systemic blood pressure and slowing of cardiac rate with increase of the intrasinal pressure, and the reverse with a decrease in intrasinal pressure.

When abnormal sensitivity of the carotid sinus reflex exists in man the evidence indicates that there is an increase in the afferent impulses. This results in a variety of symptoms of overactivity of the autonomic system depending upon which of the efferent pathways are implicated. In persons more severely afflicted syncope may be one of the symptoms.

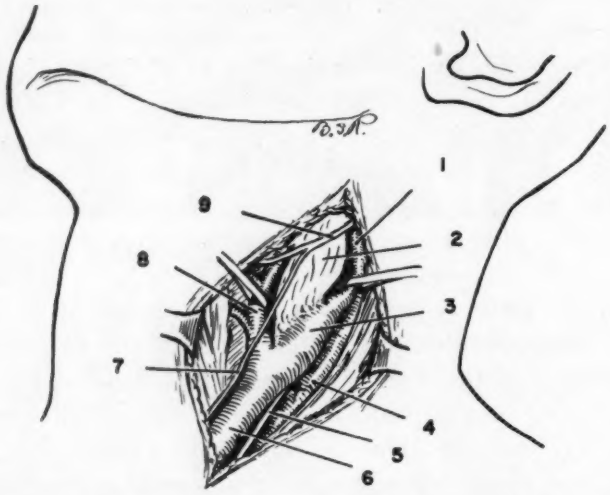


Fig. 1.—Dissection of the carotid sinus. *1*, Internal carotid artery; *2*, nerve fibers to carotid sinus; *3*, carotid sinus; *4*, internal jugular vein; *5*, vagus nerve; *6*, common carotid artery; *7*, descending hypoglossal nerve; *8*, external carotid artery; *9*, hypoglossal nerve.

The syncopal attacks may occur without warning or be preceded by such symptoms as dizziness (rarely vertigo), paresthesias in the extremities, blurring of vision, weakness, confusion, sleepiness, and epigastric distress. The syncope is usually associated with hyperpnea, successive pallor and flushing of the face, perspiration, falling, convulsive movements, varying degrees of decline in blood pressure, slowing of the cardiac rate, and irregularity of cardiac rhythm. The attacks may last a few seconds to several minutes and recovery is usually prompt. The precipitating factors cannot always be discovered but often the attacks result from sudden turning of the head or pressure on the neck. The attacks most often occur while persons are in the erect or sitting position and rarely while in the recumbent position. The frequency and severity of the attacks vary greatly even in the same individual. The syndrome is more common in middle-aged and elderly persons, and among those

afflicted is a high incidence of associated disorders, the most common of which are emotional instability, peptic ulcer, vascular hypertension, arteriosclerosis, angina pectoris, syphilis, cervical lymphadenopathy, and digitalis intoxication. The diagnosis is made from the history and from the reproduction of the attack by pressure over the abnormal carotid sinus.

The syncope which results from stimulation of the carotid sinus nerves occurs through one of three mechanisms.[5, 17] Thus, the syndrome can be divided into types on the basis of changes in the cardiac rate and the blood pressure and on the effect of certain drugs on these manifestations during stimulation of the carotid sinus: (1) the "vagal type" in which syncope results from cerebral anoxia due to reflex cardiac asystole, (2) the "depressor type" in which syncope results from cerebral anoxia due to fall in systemic blood pressure, and (3) the "cerebral type" in which syncope ensues without any significant change in cardiac rate or in blood pressure or possibly without change even in cerebral blood flow.

EXPERIENCES WITH THE CAROTID SINUS REFLEX IN SURGICAL CASES

A review of experiences with a few selected cases subjected to operation will serve best to illustrate various normal and abnormal activities of the carotid sinus reflex and also to indicate the significance of this reflex in the field of surgery.

A. Four Cases of Hypersensitive Carotid Sinus Reflex (Vagal Type) in Which the Sinus Was Denervated.

CASE 1.—O. R., a 58-year-old retired locomotive engineer, complained of recurring attacks of syncope for seven years.

He had been found by serologic tests to have syphilis and had received intensive treatment for four years. He had a cerebral vascular accident at the age of 55 which left a faint residual left-sided weakness. He had a few attacks characterized by dyspnea and mild precordial pain, thought to be angina pectoris, for one year.

The first attack of syncope had occurred seven years before. While leaning out the cab window of a locomotive he suddenly lost consciousness and fell. Since then similar attacks had occurred, first on an average of once a month, more recently as often as several times a day. He related his syncope to no constant factor unless it be to sudden turning of the head in one or another direction. The attacks often occurred without warning but sometimes were preceded by blurring of vision and a sensation as though his heart had stopped. If standing, he was likely to fall; if seated, he remained seated; no attacks occurred in recumbency. His unconsciousness lasted for an estimated time of six to twenty seconds and on return of consciousness he noted forceful heart action, profuse sweating, and a sense of weakness which often lasted for thirty minutes.

The physical examination revealed generalized arteriosclerosis of moderate degree. The carotid arteries were enlarged, more especially on the right. The heart was slightly enlarged to the left but otherwise was normal. Blood pressure averaged 156/70 and the cardiac rate 80.

The electrocardiogram showed normal rhythm and left axis deviation, probably indicative of moderate hypertrophy of the left ventricle. Otherwise the form of the tracing was essentially normal.

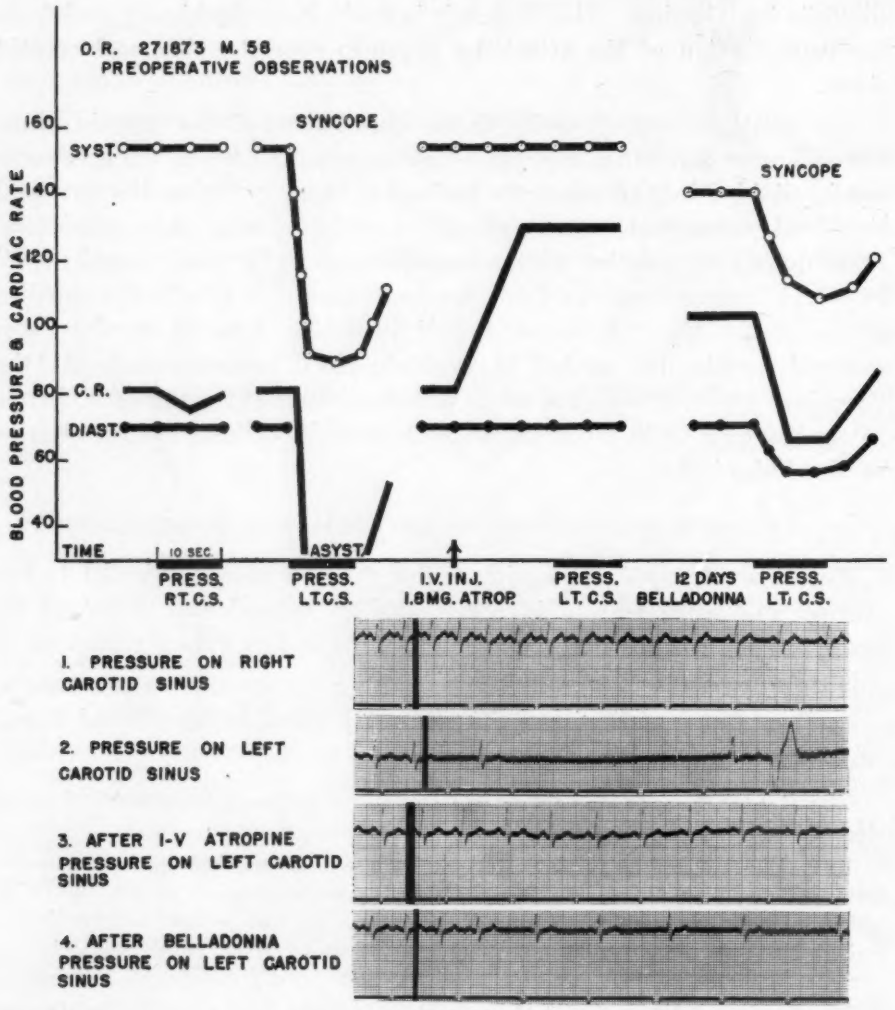


Chart 1 (Case 1).—Graphic representation of the changes observed in the preoperative tests as listed in the text. The simultaneous electrocardiographic records demonstrate the effects of the various tests on cardiac rate and rhythm. The solid black line from the top to the bottom of the electrocardiographic tracing indicates the application of pressure to the carotid sinus. The time intervals are 0.04 of a second; the Jacquet marker indicates seconds.

Special tests showed (Chart 1): (a) pressure over the right carotid sinus, no essential change in blood pressure, cardiac rate, or state of consciousness; (b) pressure over the left carotid sinus, marked drop in blood pressure, asystole for four seconds with resumption of slow abnormal contractions before release of the pressure and complete syncope; (c) after intravenous injection of atropine, all effects of pressure on the sinus were abolished; (d) after twelve days of belladonna in sufficient amounts to cause blurred vision, dry mouth, and pulse rate of 102; pressure on the left carotid sinus caused less change in blood pressure and cardiac rate than formerly but the same degree of syncope.

At operation ether anesthesia was employed and the left carotid arteries at the bifurcation were exposed (Fig. 1). The arteries were sclerotic, containing visible atheromatous plaques in their walls, and the internal carotid was moderately enlarged. Even with general anesthesia the carotid sinus reflex was intact and tests showed (Chart 2): (a) Pressure on the carotid sinus caused fall in blood pressure and cardiac asystole; (b) occlusion of the common carotid on two different trials diminished the intrasinal pressure and caused the reverse effects; (c) the injection of procaine into the carotid sinus nerves caused considerable rise in blood pressure and cardiac rate and abolished the reflex. The carotid sinus nerves and carotid body were excised and the blood pressure and pulse gradually returned to normal in thirty minutes.

During one year's follow-up there was no return of spontaneous attacks of syncope and no changes could be induced by pressure on the carotid sinuses.

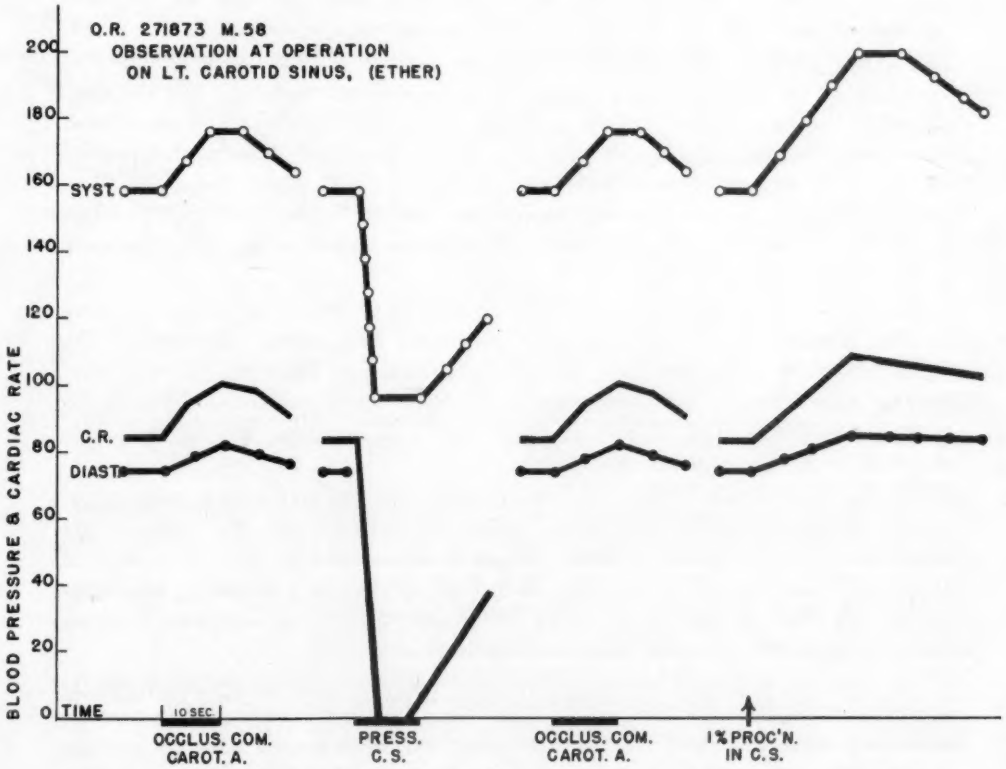


Chart 2 (Case 1).—Graphic representation of the changes observed in tests at operation on the left carotid sinus, as listed in the text.

The hypersensitive carotid sinus reflex was limited to the side on which the carotid sinus demonstrated the greater enlargement. The reflex was of the "vagal type" since the response was abolished by a suitable amount of atropine given intravenously, but the failure of atropine to prevent syncope when given in smaller doses by mouth is significant. It indicates that in the more severe cases, at least, atropine is of no value therapeutically and it has the disadvantage of producing tachycardia and a group of unpleasant symptoms.

In the observations at operation it is important to note that ether anesthesia did not affect the reflex response induced by pressure on the carotid sinus.

The increase in blood pressure and cardiac rate following reduction in intrasinal pressure induced by occlusion of the common carotid was of the same degree on repeated trials. But a reduction in intrasinal pressure of sufficient degree to produce changes equal to those resulting from interruption of the carotid sinus nerves would probably require occlusion not only of the common carotid but of the external and the distal internal carotids as well.

CASE 2.—J. P., a 68-year-old retired businessman, complained of recurring faintness for two years. He had a long history of peptic ulcer and had had a gastrojejunostomy ten years before, without complete relief of symptoms.

For two years he had recurring pain in the right side of the neck radiating to the angle of the jaw and ear, occasionally to the eye and forehead. For the same period he had beneath the angle of the right jaw a swelling which at times seemed more prominent and slightly tender. When these symptoms were most noticeable he was likely to have frequent attacks of sudden faintness. Even though he never lost consciousness he was momentarily confused and the attacks had grown so frequent that his activities were limited. He believed that smoking made him more susceptible to attacks.

The physical examination revealed general arteriosclerosis. The bulbous portions of the internal carotid arteries were prominent and almost aneurysmal; the right was more prominent than the left and tender to palpation. The cardiac findings were normal. The blood pressure averaged 116/74 and the cardiac rate 68.

The electrocardiogram showed moderate left axis deviation, but on the whole the form of the tracing was normal.

Special tests showed (Chart 3): (a) pressure over the left carotid sinus, slight change in blood pressure and cardiac rate; (b) pressure over the right carotid sinus, marked drop in blood pressure, asystole for six seconds with resumption of slow rate before release of pressure, and complete syncope preceded by numbness in the left lower extremity; (c) after intravenous injection of atropine all effects of pressure on either carotid sinus were abolished.

At operation a limited amount of procaine was employed locally and the right carotid arteries at the bifurcation were exposed. The vessels were slightly sclerotic and the bulbous portion of the internal carotid was twice normal size. On manipulation of the arteries pain similar to that complained of prior to operation occurred in the neck, jaw, and behind the ear. Stimulation of the walls of the carotid arteries with a faradic current produced a localized pain which did not radiate. This stimulation caused no change in blood pressure, cardiac rate, or state of consciousness. Other tests showed (Chart 4): (a) Pressure on the carotid sinus caused fall in blood pressure, cardiac asystole, and syncope; (b) occlusion of the common carotid caused rise in blood pressure and cardiac rate, while sudden release of the occlusion, by virtue of sudden increase in intrasinal pressure, caused temporary fall in pressure and cardiac rate below the normal; (c) procaine injected into the carotid sinus nerves caused moderate rise in blood pressure and cardiac rate and abolished the reflex. The carotid sinus nerves and carotid body were excised and the blood pressure and cardiac rate gradually returned to normal after six hours.

During eight months' follow-up there were no spontaneous attacks of syncope and no changes could be induced by pressure on the right carotid sinus. Pressure on the left carotid sinus produced the same moderate changes as occurred originally.

Carotodynia appeared to accompany the hypersensitive carotid sinus reflex and probably both were the result of local pathology in the carotids. Manipulation and faradic stimulation of the walls of the carotids readily demonstrated their pain sensitivity.

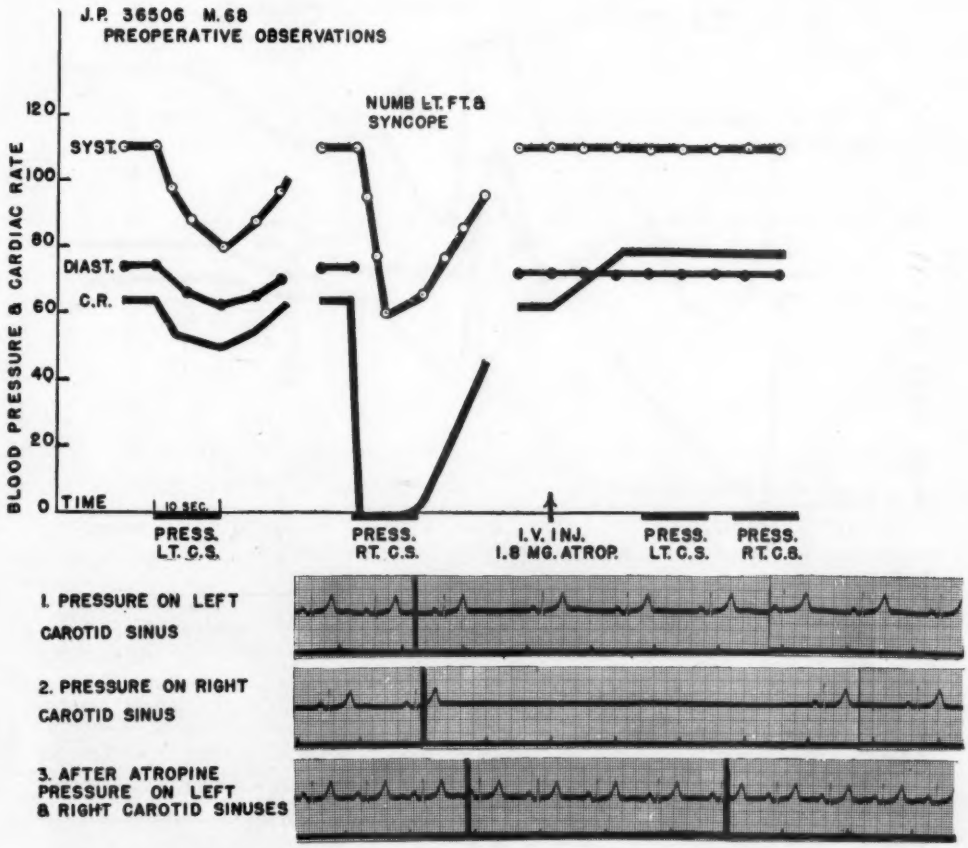


Chart 3 (Case 2).—Graphic representation of the changes observed in the preoperative tests, as listed in the text. The simultaneous electrocardiographic records demonstrate effects of the various tests on cardiac rate and rhythm.

In the other observations at operation it is significant that the increase in blood pressure and cardiac rate following sudden occlusion of the common carotid was of greater degree than that which occurred after injection of procaine into the carotid sinus nerves. This is in keeping with the frequent observation that in the carotid sinus reflex the degree of the response is in direct proportion to the suddenness and the amount of pressure on the carotid sinus. The lesser response with an-

esthetization of the sinus nerves may be accounted for by the slower interruption of the afferent stimuli, thus affording time for compensatory reactions.

CASE 3.—P. E., a 58-year-old stationary engineer, complained of recurring syncope for six months. He had a seven years' history of mild symptoms of peptic ulcer made worse by alcohol and overindulgence in tobacco. A lesion presumed to be a chancre had been treated locally by cautery in 1910; the serologic tests for syphilis were normal subsequently.

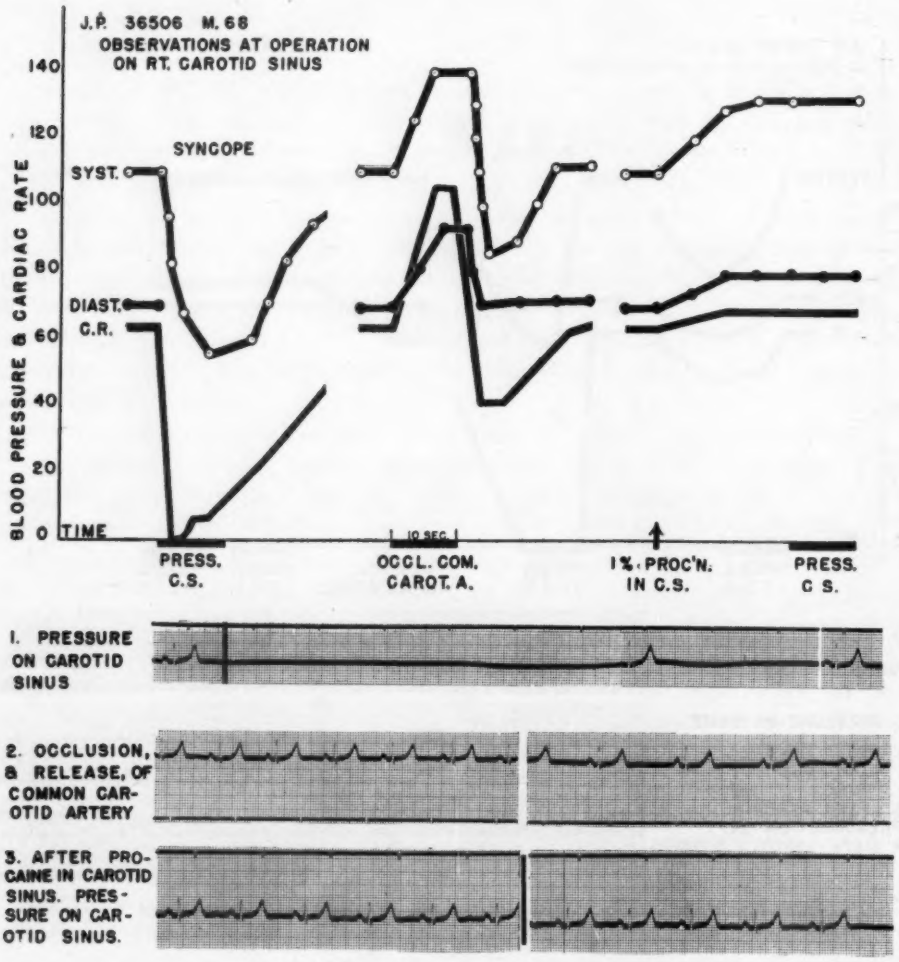


Chart 4 (Case 2).—Graphic representation of the changes observed in tests at operation on the right carotid sinus, as listed in the text. The simultaneous electrocardiographic records demonstrate effects on cardiac rate and rhythm of the various tests.

For six months he had a succession of attacks of sudden faintness when leaning over to tie his shoes, leaning over the wash bowl, and on turning his head to the left. The attacks occurred on several different occasions when on entering his house he turned to hang his hat on a hook to his left. Although the attacks never progressed to total loss of consciousness or falling, they were distressing and made him fearful at his work about machinery.

The physical examination revealed generalized arteriosclerosis of moderate degree. The common carotid arteries were prominent and the bulbous portions of the internal carotids were enlarged. The cardiac findings were normal. The blood pressure averaged 120/70 and the cardiac rate 65.

The electrocardiogram showed normal rhythm and slight left axis deviation, probably associated with beginning hypertrophy of the left ventricle. But the form of the tracing was essentially normal.

Special tests showed (Chart 5): (a) pressure over the right carotid sinus, slight drop in blood pressure and slowing of cardiac rate; (b) pressure over left carotid

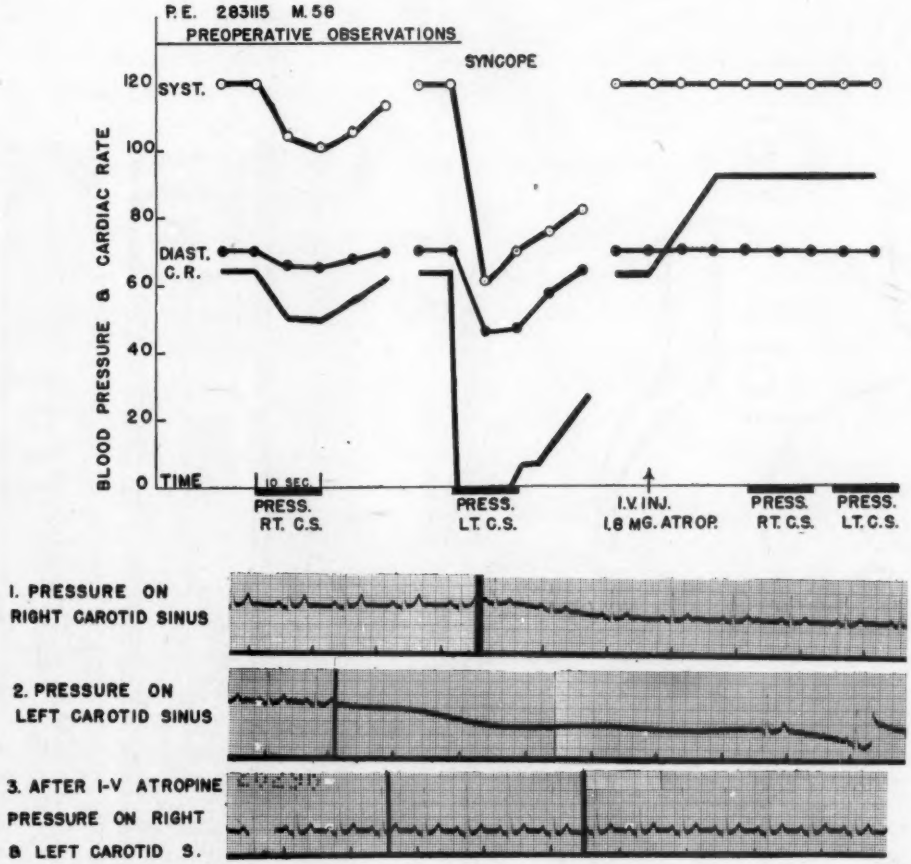


Chart 5 (Case 3).—Graphic representation of the changes observed in the preoperative tests as listed in the text. The simultaneous electrocardiographic records demonstrate the effects of the various tests on cardiac rate and rhythm.

sinus, marked drop in blood pressure, cardiac asystole for six and one-half seconds with resumption of slow rate before release of pressure, and complete syncope; (c) after intravenous injection of atropine all effects of pressure on either carotid sinus were abolished.

At operation a limited amount of procaine was employed locally and the left carotid arteries at the bifurcation were exposed. The vessels were markedly sclerotic and almost rigid and the internal carotid was enlarged. Tests showed (Chart 6): (a) Occlusion of the internal carotid 4 cm. above the bifurcation caused moderate fall in blood pressure and slowing of cardiac rate; (b) occlusion of the common carotid produced no change; (c) pressure on the carotid sinus caused marked drop

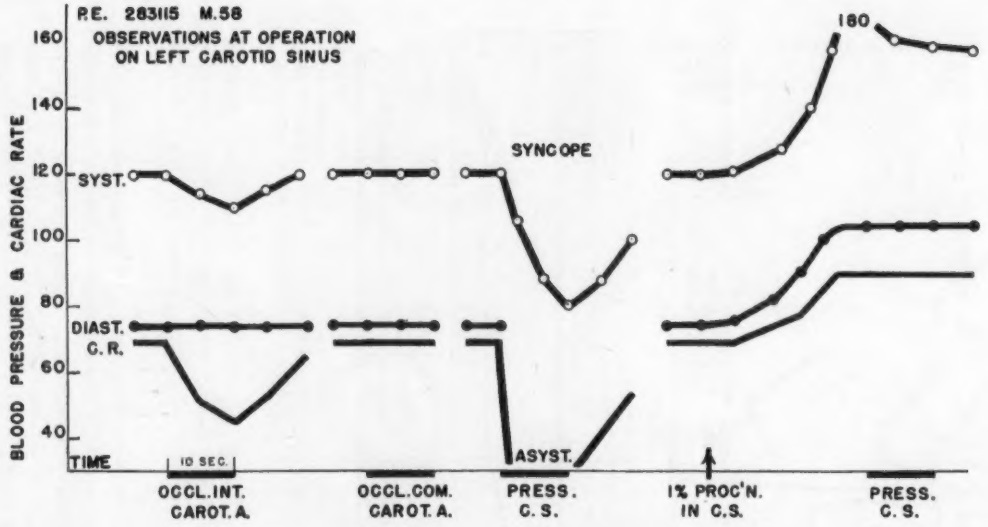
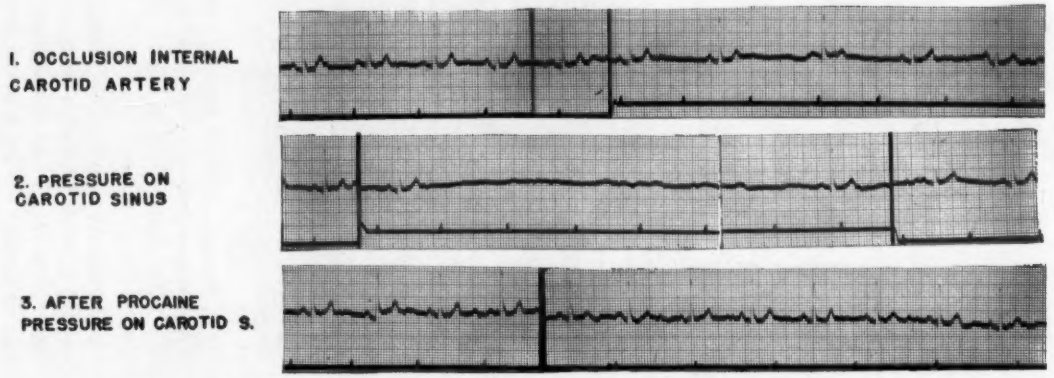


Chart 6 (Case 3).—Graphic representation of the changes observed in tests at operation on the left carotid sinus, as listed in the text. The simultaneous electrocardiographic records demonstrate effects of the various tests on cardiac rate and rhythm.



in blood pressure, cardiac asystole and syncope; (d) injection of procaine into the carotid sinus nerves caused marked rise in blood pressure and moderate rise in cardiac rate and abolished the reflex. The carotid sinus nerves and carotid body were excised and the blood pressure and cardiac rate gradually returned to normal in one-half hour.

During ten months' follow-up there were no spontaneous attacks of syncope and no changes could be induced by pressure on the denervated carotid sinus. Pressure on the opposite sinus produced the same moderate changes as occurred originally.

At least two of the observations at operation are of interest. One, occlusion of the internal carotid 4 cm. above the bifurcation, stimulated the sinus reflex. Whether the stimulation occurred by direct pressure on nerve endings that extend above the bulbous portion of the internal carotid or by increasing the intrasinal pressure cannot be determined. But it was demonstrated by pressure tests in this and at least one other case that the carotid sinus nerve endings do not extend down into the wall of the common carotid any appreciable distance.

The other observation of interest is the absence of effect on lowering the intrasinal pressure by occlusion of the common carotid, yet a marked effect on anesthetization of the carotid sinus nerves. The most tenable explanation is that in the presence of a very sclerotic and rigid arterial wall the effects of lowering the intrasinal pressure are nullified by the failure of the sinus to collapse.

CASE 4.—H. L., a 59-year-old retired fireman, complained that when anything pressed, even gently, on the right side of his neck he fainted.

He had had a carcinoma of the lower lip on the right side excised surgically on two occasions in the previous six years. There was a question of metastasis to the cervical nodes and he had been concerned about palpable nodes in his neck, especially on the right side.

For about eight months he had found that palpation of the right side of his neck just beneath the jaw by physicians or by himself almost always resulted in an attack of faintness with either partial or complete loss of consciousness. Pressure here from shaving or from a collar also induced the attacks but as long as no pressure occurred there were no attacks.

The physical examination revealed the scar of an apparently cured lesion of the lower lip on the right. There was considerable oral infection due to decayed teeth and a number of nontender cervical nodes on both sides of the neck but most pronounced on the right. The carotid arteries on both sides of the neck were prominent. There was a moderate degree of generalized arteriosclerosis. The cardiac findings were normal but for slight enlargement of the heart to the left. The blood pressure was 164/90 and the cardiac rate 80.

The electrocardiogram showed normal sinus rhythm and moderate left axis deviation. The form of the tracing was essentially normal.

Special tests showed (Chart 7): (a) pressure over the left carotid sinus, a decided fall in blood pressure and cardiac rate, and slight syncope; (b) pressure on the right carotid sinus, marked drop in blood pressure, cardiac asystole with a few abnormal contractions occurring during the period of pressure, and simultaneous loss of consciousness with convulsive movements of the extremities more marked on the

left; (c) after intravenous injection of atropine all effects of pressure on the carotid sinuses were abolished but for slight bradycardia following pressure on the right sinus.

At operation ether anesthesia was employed and the right carotid arteries at the bifurcation were exposed after radical dissection of the neck and excision of nodes had been performed. The carotids were moderately sclerotic. Tests showed (Chart 8): (a) Occlusion of the internal carotid 4 cm. above the bifurcation caused slight drop in blood pressure and in the cardiac rate; (b) occlusion of the common carotid caused but slight rise in blood pressure; (c) pressure on the carotid

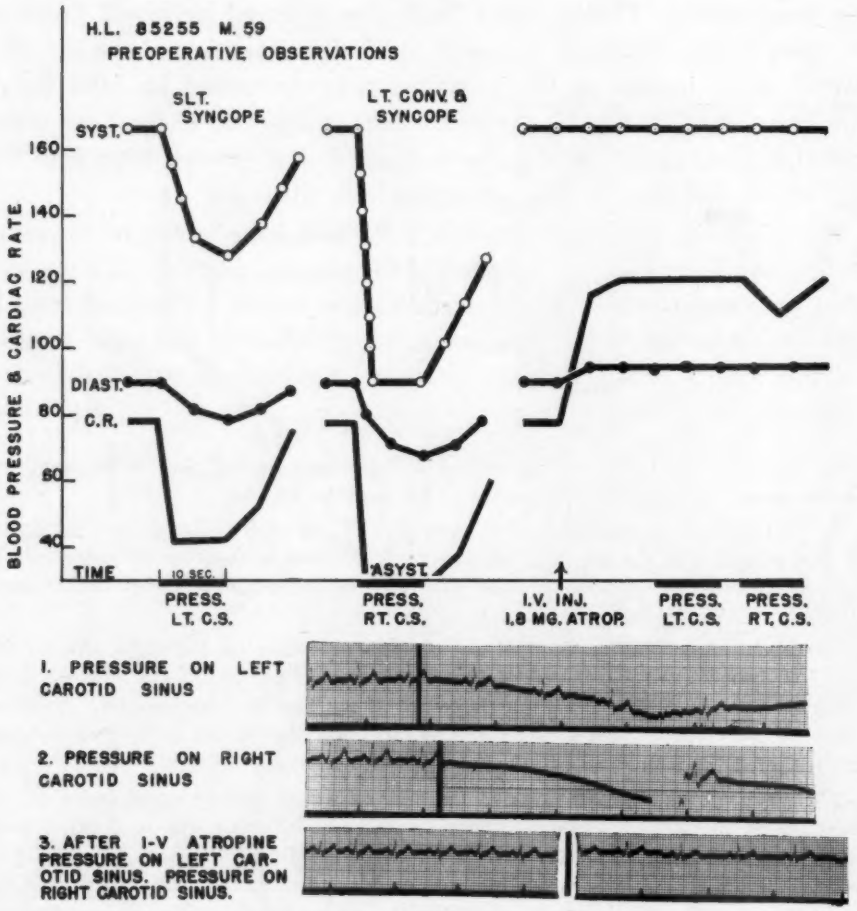


Chart 7 (Case 4).—Graphic representation of the changes observed in the preoperative tests as listed in the text. The simultaneous electrocardiographic records show the effects of the various tests on cardiac rate and rhythm.

sinus caused marked fall in systolic pressure and marked slowing of the cardiac rate; (d) injection of procaine into the carotid sinus nerves caused only slight rise in systolic pressure and abolished the reflex. The carotid sinus nerves and carotid body were excised. The cervical nodes were inflammatory.

During eight months' follow-up no spontaneous syncope occurred and no changes followed pressure over the right carotid sinus.

In this case the carotid sinus reflex was hypersensitive on both sides but much more accentuated on the right. In the preoperative tests it is interesting that with stimulation of the sinus reflex on the right there occurred convulsive movements only on the left. This would suggest that changes occurred in the right cerebrum to cause the convulsions, yet when the effects of the reflex on the systemic blood pressure and

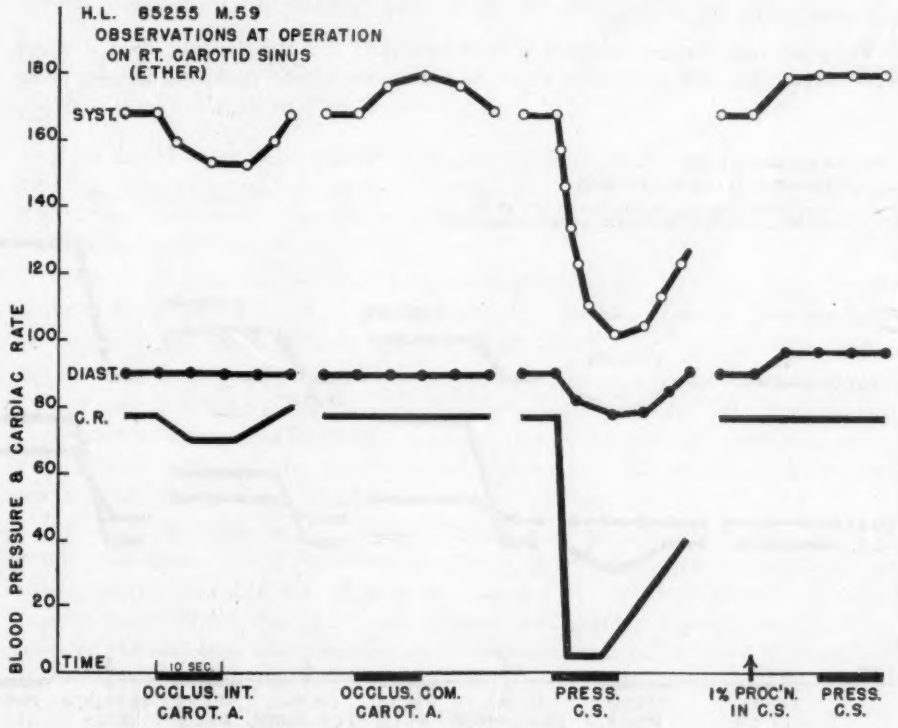


Chart 8 (Case 4).—Graphic representation of the changes observed at operation on the right carotid sinus, as listed in the text.

the cardiac rate were abolished by intravenous atropine the convulsions, as well as the syncope, failed to develop also. Since the effect of atropine is assumed to be peripheral, and the origin of the convulsions was central, the abolition of the convulsions by injection of atropine is a paradox which is not readily explained.

The rise in blood pressure was slight and change in cardiac rate nil after anesthetization of the carotid sinus nerves which suggests that in people with hypertension interruption of the afferent part of one carotid sinus reflex may be accompanied by little change in blood pressure.

B. Case of Hypersensitive Carotid Sinus Reflex (Cerebral Type) Associated With Tuberculous Nodes in the Neck in Which Cure Followed Excision of the Nodes.

CASE 5.—S. D'A., a 40-year-old plumber, complained of recurring swelling in the neck and of fainting attacks.

He had had recurring tuberculous nodes in the neck for about ten years, treated with numerous local excisions. For the past six months several fairly large painless swellings had existed beneath the angle of the right jaw. For three months he had daily attacks of syncope heralded by a full feeling in the head, dizziness, and general weakness. He never lost consciousness and never fell but was confused for eight to ten seconds and following this broke out in perspiration, especially about the face, and felt nauseated. The attacks usually occurred while he was standing but occasionally while sitting.

Physical examination revealed a well-nourished healthy looking man. There were several palpable nontender nodes in both sides of the neck, the largest being

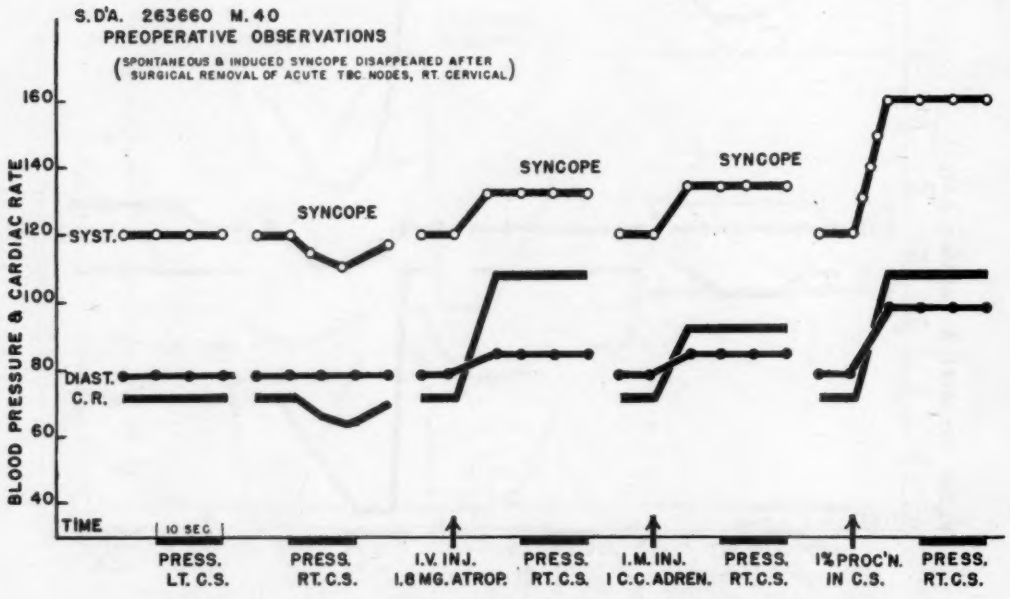


Chart 9 (Case 5).—Graphic representation of the changes observed in the preoperative tests as listed in the text.

about 2½ cm. in diameter and lying just over the right carotid sinus. There was no active pulmonary tuberculosis. The cardiac findings were normal. The blood pressure was 120/80 and the cardiac rate 70.

Special tests showed (Chart 9): (a) pressure over the left carotid sinus, no effects; (b) pressure on the node over the right carotid sinus, only slight fall in systolic pressure and cardiac rate but complete syncope; (c) intravenous injection of atropine abolished the effects on blood pressure and cardiac rate but not the syncope following pressure on the right carotid sinus; (d) intramuscular injection of adrenalin had essentially the same effects as injection of atropine; (e) injection of procaine into the right carotid sinus caused a rise in blood pressure and cardiac rate and syncope did not occur with pressure over the sinus.

At operation the larger cervical nodes on the right side were excised locally and no observations were made on the carotid sinus reflex at the operation.

During one year after operation there were no spontaneous attacks of syncope and none could be induced by pressure on the carotid sinuses.

The "cerebral type" of syncope occurring with a hypersensitive carotid sinus reflex is the most interesting of the three types of syncope. Its mechanism is not at all clear since there are no demonstrable changes in blood pressure or cardiac rate and some deny the existence of this type of syncope. If it does exist unqualifiedly it is the only example in which loss of consciousness alone occurs from the stimulation of afferent nerves. In the study of this patient every effort was made to avoid suggestion or making him aware of anticipated phenomena.

C. Two Cases Illustrating Reactions of the Normal Carotid Sinus Reflex When Examined at Operation.

CASE 6.—M. L., a 16-year-old girl, had a verified congenital arteriovenous anomaly existing principally in the pial vessels over the left parietal cerebral hemisphere. The lesion caused local convulsive seizures in the right extremities without loss of consciousness.

Physical examination revealed a cephalic bruit on the left and slight impairment of sensation on the right side of the body. In other respects she appeared to be normal. The blood pressure was 110/60 and the cardiac rate 80. The form of the electrocardiogram was normal.

The carotid arteries in the neck were not remarkable on palpation. Pressure over each carotid sinus caused slight fall in systolic pressure and slight slowing of cardiac rate. Pressure on the left carotids caused diminution in the cephalic bruit and this was the indication for carotid ligation.

At operation procaine was employed locally and the left carotid arteries at the bifurcation were exposed. The arteries were slightly larger than average but otherwise appeared normal. Tests showed that (Chart 10): (a) Occlusion of the common carotid caused slight rise in systolic pressure and cardiac rate and on sudden release of the occlusion there was prompt return to normal but no drop in blood pressure or slowing of cardiac rate below the original level; (b) pressure on the carotid sinus caused slight fall in systolic pressure and slowing of cardiac rate; (c) gradual injection of procaine into the carotid sinus nerves (followed by ligation of the common carotid artery) caused moderate rise in blood pressure and in cardiac rate with return to normal in ten minutes. There were no untoward effects from ligation of the carotid.

CASE 7.—M. B., a 19-year-old boy, had a verified congenital arteriovenous anomaly existing largely in the pial vessels over the right parietal cerebral hemisphere. This lesion caused local convulsive seizures in the left extremities without loss of consciousness.

Physical examination revealed a cephalic bruit of low intensity and slight changes in the reflexes on the left side of the body. In other respects he appeared to be a normal healthy boy. The cardiac findings were normal. The blood pressure was 115/75 and the cardiac rate 64. The form of the electrocardiogram was essentially normal.

The carotid arteries in the neck were not remarkable and repeated pressure over the carotid sinuses failed to produce any change in blood pressure, the cardiac rate, or the state of consciousness. Occlusion of the right carotids did, however, diminish the cephalic bruit and this was the indication for carotid ligation.

At operation procaine was employed locally and the right carotid arteries at the bifurcation were exposed. The vessels and adjacent structures were of normal appearance. Tests showed that (Chart 11): (a) Occlusion of the common carotid caused prompt and marked rise in blood pressure and cardiac rate with return to

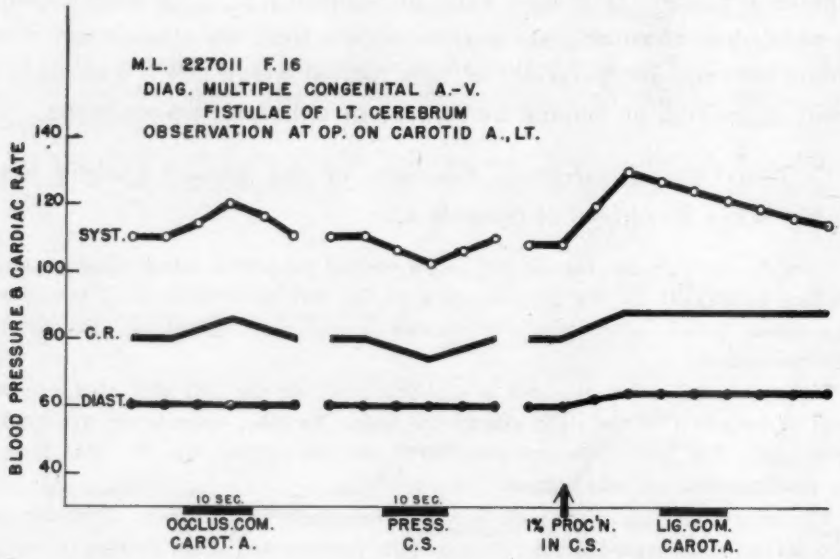


Chart 10 (Case 6).—Graphic representation of the changes observed at operation on direct stimulation of a normal carotid sinus, as listed in the text.

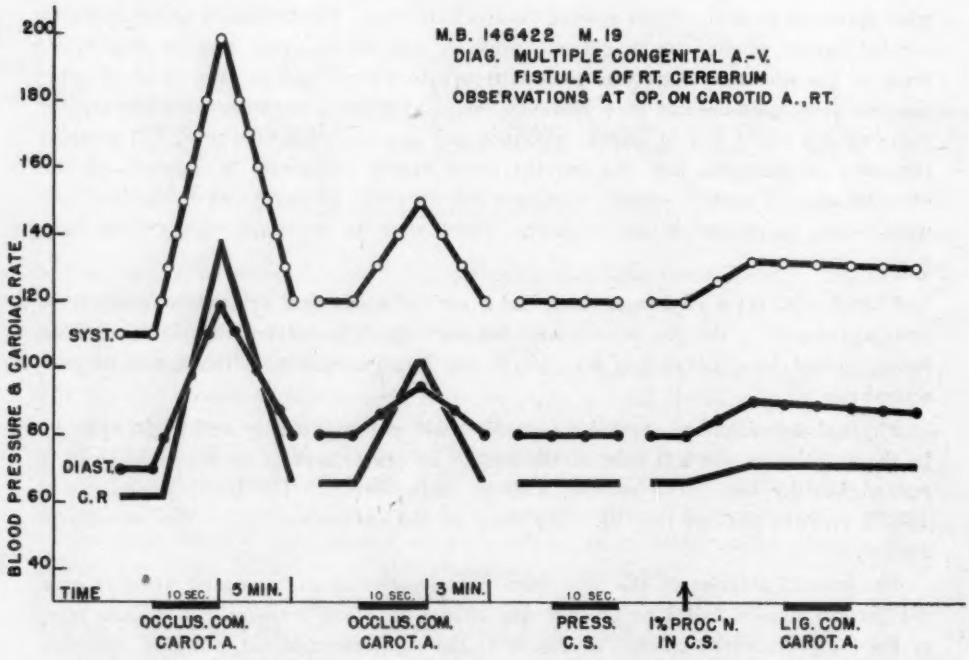


Chart 11 (Case 7).—Graphic representation of the changes observed at operation on direct stimulation of a normal carotid sinus, as listed in the text.

normal five minutes after release of the occlusion; (b) repetition of the occlusion of the common carotid caused the same type of response as before but of less degreee; (c) pressure on the carotid sinus caused no changes; (d) injection of procaine into the carotid sinus nerves (followed by ligation of the common carotid) caused only a moderate rise in blood pressure and cardiac rate with return to normal in fifteen minutes. There were no untoward effects from the ligation of the carotid.

While many tests have been made on the effects of pressure on the normal carotid sinus there is limited opportunity to employ direct tests on the normal sinus that has been exposed at operation. In Cases 6 and 7 there are lesions of the cerebral vasculature but it is reasonable to assume that the carotid sinus reflex in each is normal. The responses of the normal carotid sinus are thought to be variable within limits and the responses in these two cases are confirmatory.

The responses in Case 6 probably represent those existing in the majority of people with a normal carotid sinus reflex. In Case 7 the absence of hypersensitivity of the sinus reflex is demonstrated by the lack of response on direct pressure on the sinus. The marked rise in blood pressure and cardiac rate on sudden reduction of intrasinal pressure by occlusion of the common carotid can be considered normal though not constant in all cases. The fact that a repetition of the test shortly after gave a response of less degree, and that after a few minutes interruption of the reflex by anesthetization of the carotid sinus nerves gave little response at all, indicates the sustained effects of compensatory mechanisms once they are induced.

D. Case Illustrating Syncope Due Not to Hypersensitive Carotid Sinus Reflex But to Arterial Occlusion Alone.

CASE 8.—C. E., a 61-year-old woman, struck her head in a fall resulting in an arteriovenous fistula between the intracranial portion of the internal carotid artery and the cavernous sinus on the right. She suffered from headache and loss of motion in the right eye.

Physical examination revealed complete ophthalmoplegia, impaired vision, and periorbital edema on the right. There was a loud cranial bruit and general arteriosclerosis of moderate degree. The heart was normal, the blood pressure 110/70, and the cardiac rate 68.

Ligation of the carotids in the right side of the neck was planned as a therapeutic measure. However, trial occlusion of the right carotids always resulted in prompt loss of consciousness and convulsive movements on the left side of the body. Since the patient's neck was short and thick it was never possible to determine definitely whether any pressure sufficient to occlude the common carotid alone might not at the same time be stimulating the carotid sinus reflex as well.

Special tests showed that (Chart 12): (a) Pressure on the left carotid sinus caused no changes; (b) pressure on the right carotid sinus caused syncope and left convulsive movements but no change in blood pressure or cardiac rate; (c) after intravenous injection of atropine, pressure on the right carotid sinus caused the same

response as before; (d) after injection of procaine into the right carotid sinus nerves syncope still followed pressure over the right carotid sinus.

The observations demonstrated the responsibility for syncope following pressure on the carotids to rest wholly in the cerebral anoxia due to carotid occlusion. Thus, therapeutic ligation of the carotids was shown to be unsafe.

This case illustrates the usefulness of employing tests to demonstrate the presence or absence of a hypersensitive carotid sinus reflex. Doubtless therapeutic carotid ligation has been denied patients in the past because syncope occurred with trial occlusion of the carotids by pressure on the neck when exclusion of the carotid sinus reflex would have indicated the safety of the ligation.

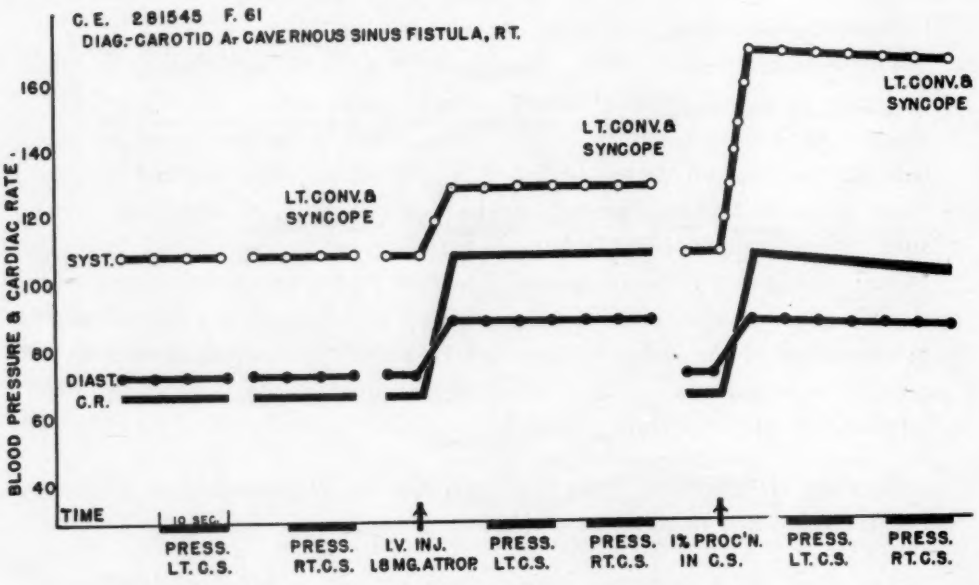


Chart 12 (Case 8).—Graphic representation of the changes observed in the tests, as listed in the text.

E. Five Cases Illustrating the Variable Role of the Glossopharyngeal Nerve in the Transmission of the Afferent Impulses From the Carotid Sinus.

Case 9.—M. K., a 63-year-old man, had intractable pain from carcinoma and osteomyelitis of the right mandible. There was little generalized arteriosclerosis. The heart was normal. Blood pressure was 130/80 and the cardiac rate 80. Section of the fifth and ninth cranial nerves was advised for relief of pain.

At operation ether anesthesia was employed and the right glossopharyngeal nerve was cut intracranially. In the ten minutes following, the blood pressure rose steadily from 130/80 to a level of 160/95, then gradually returned to normal in the next fifteen minutes. In the same period the pulse rate rose and fell ten points. The postoperative blood pressure and pulse rate were the same as the preoperative.

CASE 10.—C. Y., a 61-year-old man, had intractable pain from carcinoma involving the right maxilla, mandible, and pharynx. There was a moderate degree of generalized arteriosclerosis. The heart was normal. The blood pressure was 130/80 and the cardiac rate 80. Section of the fifth, ninth, and tenth cranial nerves and upper cervical sensory roots was advised for relief of pain.

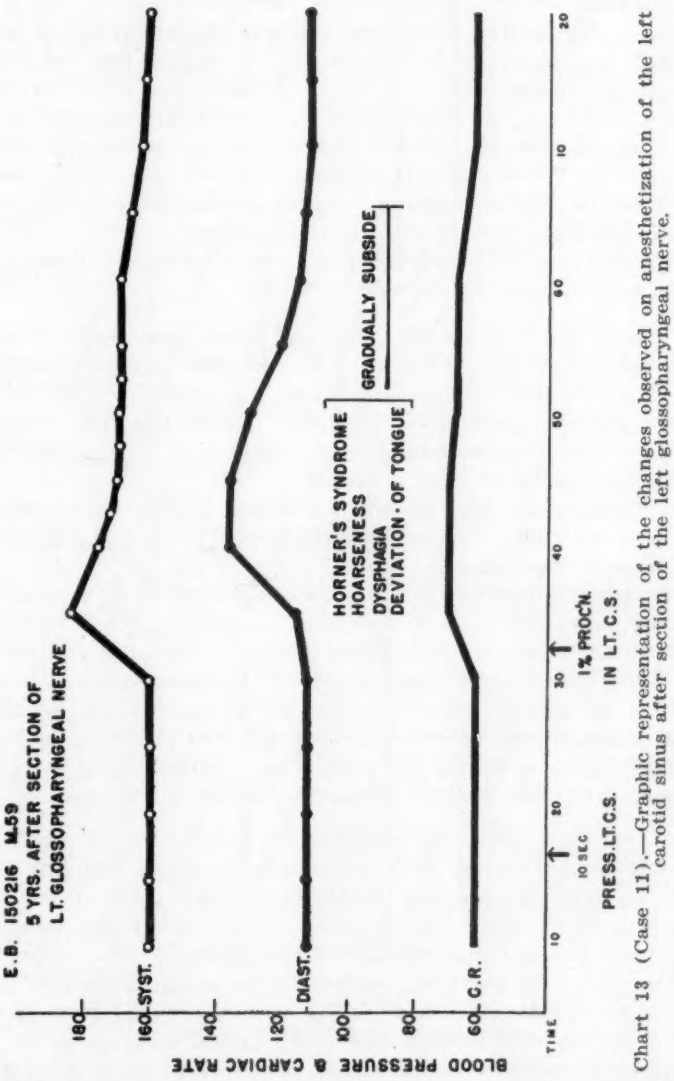


Chart 13 (Case 11).—Graphic representation of the changes observed on anesthetization of the left carotid sinus after section of the left glossopharyngeal nerve.

At operation procaine was employed locally and the right glossopharyngeal nerve was cut intracranially. In the ten minutes following, the blood pressure rose from 120/75 to 130/75, then gradually returned to the original level in the next fifteen minutes. In the same period the pulse rate rose and fell eight points. When the vagus nerve was cut intracranially later there was an accompanying rise in pulse rate of twenty points, but no change in blood pressure. The postoperative blood pressure and pulse rate were the same as the preoperative.

CASE 11.—E. B., a 59-year-old man, had paroxysmal pain characteristic of glossopharyngeal neuralgia on the left. His general physical condition was good. The heart was normal. Blood pressure was 138/70 and cardiac rate 78.

At operation avertin and ether were employed and the left glossopharyngeal nerve was cut intracranially. In the next six minutes the blood pressure rose from 110/70 to a level of 135/75, then gradually returned to its original level in the next twenty minutes. In the same period the pulse rose twelve points. The postoperative blood pressure and pulse rate were the same as the preoperative.

Five years after section of the left glossopharyngeal nerve, pressure over the right carotid sinus caused marked slowing of the cardiac rate and drop in blood pressure but no syncope, while pressure on the left sinus caused no effects. Anesthetization of the left carotid sinus with 15 c.c. of 1 per cent procaine (Chart 13) caused prompt rise in systolic pressure of twenty-five points and in diastolic pressure of twelve points. The cardiac rate increased but six points. There was a gradual return of blood pressure to normal in forty-five minutes, during which the effects of the procaine subsided. This response indicated an intact carotid sinus reflex. Accompanying symptoms of anesthetizing the area were a left Horner's syndrome, hoarseness, and deviation of the tongue to the left.

CASE 12.—G. H., a 58-year-old man, had paroxysmal pain characteristic of glossopharyngeal neuralgia, on the left. He had generalized arteriosclerosis. The heart was not enlarged but the cardiac rate was irregular. The blood pressure was 110/80 and the cardiac rate 120. The electrocardiogram showed auricular fibrillation and complexes indicating myocardial damage. After digitalization the cardiac rate and rhythm returned to normal.

At operation procaine was employed locally and the left glossopharyngeal nerve was cut intracranially. This was unaccompanied by any significant change in cardiac rate or in blood pressure.

One year after section of the left glossopharyngeal nerve, pressure over either carotid sinus caused no appreciable effects. Anesthetization of the left carotid sinus with 10 c.c. of 1 per cent procaine (Chart 14) caused prompt rise in systolic pressure of fifty points and in diastolic pressure of sixteen points. The cardiac rate increased but five points. There was a gradual return of blood pressure to normal in thirty-five minutes, during which the effects of the procaine subsided. This response indicated an intact carotid sinus reflex. Accompanying symptoms of anesthetization of the area were left Horner's syndrome and hoarseness.

CASE 13.—G. C., a 40-year-old woman, had had the fifth and ninth cranial and the first four cervical sensory roots cut intradurally on the left side for neuralgia of unknown origin. In addition, examination showed palsy of the eleventh and twelfth nerves on the left. The operation had been performed elsewhere and the record of pulse rate and blood pressure during operation was not available. The heart was normal. The blood pressure was 130/80 and the pulse rate 70.

Eighteen months after section of the left glossopharyngeal nerve (plus paralysis of the left hypoglossal) pressure over either carotid sinus caused no appreciable effects. Anesthetization of the left carotid sinus with 20 c.c. of 1 per cent procaine caused a left Horner's syndrome, hoarseness, dysphagia, and tachycardia but no change in blood pressure. This indicated the absence of an intact carotid sinus reflex.

Anatomically the connections of the nerves to the carotid sinus have been shown to be with the ninth, tenth, and twelfth cranial nerves and the cervical sympathetics.[15] The principal nerve with which the sinus has been thought to be supplied is the ninth cranial nerve through the

"carotid sinus nerve" (nerve of Hering). On the basis of experimental denervation of the sinus in dogs it has been concluded that the cardiovascular components of the sinus reflex are conducted solely through the carotid sinus nerve.[3] Bucy[1] cited his experiences with four cases in which, with intracranial section of the ninth cranial nerve, there was a

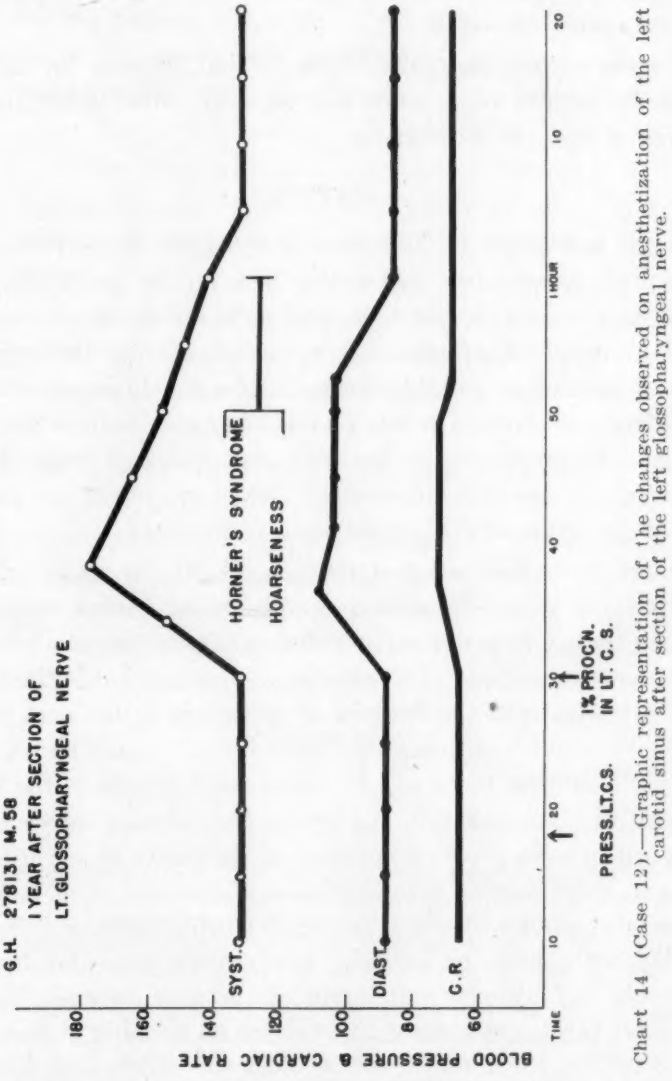


Chart 14 (Case 12).—Graphic representation of the changes observed on anesthetization of the left carotid sinus after section of the left glossopharyngeal nerve.

resultant rise in blood pressure. The conclusion which these and other observations imply is that in man the afferent impulses of the sinus reflex are conducted through the ninth cranial nerve and its branch the carotid sinus nerve.

In four cases (Cases 9 to 12) of intracranial section of the ninth cranial nerve, temporary rise in blood pressure occurred in three but there was no change in the fourth. In two cases (Cases 11 and 12)

subsequent anesthetization of the carotid sinus on the side of operation caused the characteristic rise in blood pressure that occurs with the intact reflex, indicating that the sinus reflex was qualitatively unchanged in these two. In Case 13 anesthetization of the carotid sinus on the side of operation caused no change in blood pressure but in this case there was, in addition to the section of the ninth cranial nerve, a paralysis of the twelfth cranial nerve.

These observations, therefore, indicate that in man the afferent impulses of the carotid sinus reflex are not transmitted solely through the ninth cranial nerve in all instances.

COMMENT

When the symptoms of hypersensitive carotid sinus reflex are mild or infrequent, reassurance, instruction in avoiding quick movements of the head or pressure on the neck, and mild sedatives will often suffice to avoid or minimize attacks. X-ray irradiation of the carotid sinus has been suggested as suitable treatment for the hypersensitive reflex[14] but irradiation of tumors in this region sometimes induces a hypersensitive reflex. Prolonged use of atropine, ephedrine, or comparable drugs to control symptoms is not desirable. When symptoms are more severe surgical denervation of the carotid sinus is indicated.

There are no indications that the normal carotid sinus reflex should be of itself the source of serious complications during surgical procedures, but that a hypersensitive reflex possesses potential dangers deserves wider recognition. The anesthetic management,[12] the sensitizing effect of digitalis,[5] and the dangers of operations in the neck in patients with hypersensitivity of the carotid sinus reflex[9, 16] have been emphasized by others. Doubtless there will be increasing evidence of the role of the hypersensitive sinus reflex in the production of surgical complications, many of which have gone unexplained in the past. It might be well for surgeons in their routine preoperative examinations to include pressure on the carotid sinuses of every patient. During operation, in the event of cardiac arrhythmia or asystole, bradycardia, vascular hypotension, and possibly convulsions, infiltration of the area between the external and internal carotid arteries with procaine on the side known to possess a hypersensitive sinus reflex will abolish the reflex and may possibly restore the patient.

CONCLUSIONS

1. The diagnosis of hypersensitive carotid sinus reflex is made by the patient's history and a systematic examination of the carotid sinuses.

2. Carotodynia sometimes is associated with the carotid sinus syndrome.

3. The frequency of local abnormalities of the carotid arteries and adjacent tissues on the side of the hypersensitive sinus reflex suggests that the abnormal reflex results from pathology in the sinus.

4. If symptoms of hypersensitive sinus reflex are disagreeable or incapacitating and not controlled by simple measures surgical denervation of the carotid sinus is advisable. The operation causes only transitory alteration of the cardiovascular system.

5. By anesthetizing the carotid sinus nerves it is possible to distinguish between syncope due to a hypersensitive sinus reflex and syncope due simply to cerebral anoxia resulting from carotid occlusion.

6. The glossopharyngeal nerve in man is not in every instance the only nerve through which afferent impulses of the carotid sinus reflex are transmitted.

7. Hypersensitivity of a carotid sinus reflex may play an important role in the production of cardiac arrhythmias, cardiac asystole, and fall in blood pressure occurring during operations, especially operations about the neck.

8. Ether anesthesia cannot be counted upon to abolish a hypersensitive sinus reflex.

9. Infiltration with 1 per cent procaine of the carotid sinus nerves lying in the space between the internal and external carotids always temporarily abolishes the sinus reflex. Simultaneous bilateral anesthetization of the region of the carotid sinus is not advisable because of the possible bilateral laryngeal palsy that might accompany it.

REFERENCES

1. Bucy, P.: The Carotid Sinus Nerve in Man, Arch. Int. Med. **58**: 418-432, 1936.
2. de Castro, F.: Sur la Structure et l'Innervation du Sinus Carotidien de l'Homme et des Mammifères. Nouveaux Faits sur l'Innervation du Glomus Caroticum, Trav. Lab. Recherch. Madrid **25**: 331, 1928.
3. Code, C. F., Dingle, W. T., and Moorhouse, V. H. K.: The Cardiovascular Carotid Sinus Reflex, Am. J. Physiol. **115**: 249-260, 1936.
4. Craig, W. McK., and Smith, H. L.: The Surgical Treatment of Hypersensitive Carotid Sinus Reflexes; Report of 13 Cases, Yale J. Biol. & Med. **11**: 415-422, 1939.
5. Ferris, E. B., Jr., Capps, R. B., and Weiss, S.: Carotid Sinus Syncope and Its Bearing on the Mechanism of the Unconscious State and Convulsions, Medicine **14**: 377-456, 1935.
6. Hering, H. E.: Die Karotissinusreflexe auf Herz und Gefässe vom normal-physiologischen, pathologisch-physiologischen und klinischen Standpunkt Gleichzeitig über die Bedeutung der Blutdrück zügler für den normalen und abnormen Kreislauf. Th. Steinkopff, Dresden, 1927.
7. Heymans, C.: Le Sinus Carotidien et les Autres Zones Vasosensibles Réflexogènes, London, 1929, H. K. Lewis & Co.
8. Heymans, C., and Rijlant, P.: Le Courant d'Action du Nerf du Sinus Carotidien Intact, Compt. rend. Soc. de biol. **113**: 69-73, 1933.
9. Leger, L.: Le Danger Sinu-Carotidien des Interventions Cervicales, Presse méd. **48**: 451-453, 1940.
10. Mulholland, J. H., and Rovenstine, E. A.: Surgery in Carotid Sinus Syndrome, SURGERY **9**: 751-757, 1941.

11. Robinson, L. J.: Syncope, Convulsions and Unconscious State; Relation to Hyperactive Carotid Sinus Reflex, Arch. Neurol. & Psychiat. **41**: 290-297, 1939.
12. Rovenstine, E. A., and Cullen, S. C.: The Anesthetic Management of Patients With a Hyperactive Carotid Sinus Reflex, SURGERY **6**: 167-176, 1939.
13. Smith, H. L.: Fainting Attacks Resulting From Hypersensitive Carotid Sinus Reflexes, Am. Heart J. **14**: 614-619, 1937.
14. Stevenson, C. A.: Use of Roentgen Therapy in Carotid Sinus Syndrome, Radiology **32**: 209-214, 1939.
15. Tchibukmacher, N. B.: Surgical Anatomy of the Carotid Sinus Nerve and Inter-Carotid Ganglion, Surg., Gynec. & Obst. **67**: 740-745, 1938.
16. Weese, H.: Mechanism of Anesthesia Accidents Following Intravenous Use of Evipal Soluble, Barbital Derivative, in Sublingual Phlegmons (Rôle of Carotid Sinus), Anesth. & Analg. **18**: 15-21, 1939.
17. Weiss, S., and Baker, J.: The Carotid Sinus Reflex in Health and Disease: Its Rôle in Causation of Fainting and Convulsions, Medicine **12**: 297-354, 1933.
18. Weiss, S., Capps, R. B., Jr., Ferris, E. B., Jr., and Munro, D.: Syncope and Convulsions Due to Hyperactive Carotid Sinus Reflex; Diagnosis and Treatment, Arch. Int. Med. **58**: 407-417, 1936.

VITAMIN A CONTENT OF PLASMA AND HEPATIC TISSUE BIOPSIED AT OPERATION: EFFECTS OF PREOPERATIVE THERAPY IN OBSTRUCTIVE JAUNDICE

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DURING the course of studies on the biochemical changes due to obstruction of the biliary tract, it seemed desirable to investigate possible disturbances in vitamin A metabolism. Abnormalities in vitamin A absorption, conversion, and storage in obstructive jaundice might be predicted on the basis of available evidence.[1, 2] Beta-carotene, the common vegetable source of vitamin A, like vitamin A is fat-soluble and is absorbed from the intestine with difficulty in the absence of bile salts.[2, 3] Beta-carotene and other carotenoid precursors of vitamin A apparently are converted into the vitamin in the liver, through the action of an enzyme, carotinase.[1] As shown in studies on rats, from 90 to 95 per cent of the vitamin A of the body is stored in the liver, small amounts also being found in the kidneys and lungs.[4] Storage of carotene as such occurs to only a negligible extent, however.

Conditions which influence the concentrations of vitamin A and carotenoids in the plasma are not well understood. Bessey and Wolbach[1] concluded that there is no association between the amount of carotene ingested and its level in the plasma. The question has been raised as to whether vitamin A concentration in the plasma reflects the extent of hepatic storage, for fluctuations of the plasma value may occur during acute infections. The weight of evidence seems to indicate, however, that plasma vitamin A concentration in the absence of fever is a satisfactory index of the state of vitamin A nutrition.[5, 6] From observations on sixty-two normal men and the same number of healthy women, Abels and co-workers[7] reported a plasma vitamin A range of 1.32 to 2.08 U.S.P. units per cubic centimeter for the men, and 1.03 to 1.95 for the women, the average figures being 1.70 and 1.49 respectively.

Measurements have been made by various investigators on the vitamin A concentration in the post-mortem hepatic tissue of individuals who died from acute or chronic diseases. The livers of previously healthy individuals succumbing to violence were found to have an average

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vitamin A content of 331 U.S.P. units per gram, according to Crimm and Short.[8] Ralli and collaborators[9] reported an average value from similar material of 766 U.S.P. units per gram, with a rather wide variation noted. They found much lower concentrations in cirrhotic livers, the average value being 137 U.S.P. units per gram, and in acute infections accompanied by evidence of liver damage. Fox[10] found concentrations of 12 to 938 "blue units" per gram of liver tissue in native mine workers killed in industrial accidents, the average figure being 297. Similar values were recorded by Moore.[11] All such studies have shown wide variation in the post-mortem hepatic vitamin A content, even in the livers of individuals supposedly in good health prior to fatal trauma.

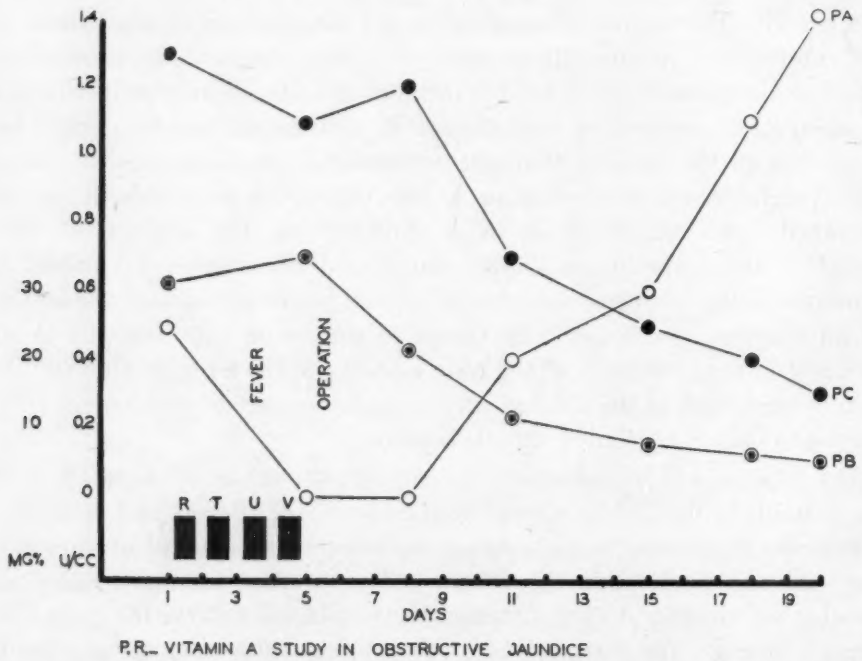


Fig. 1.—P. R., a 60-year-old man with carcinoma of the head of the pancreas and complete biliary obstruction, had cholecystgastrostomy performed under spinal anesthesia, after which the jaundice rapidly cleared. Before operation, at points marked *R*, *T*, *U* and *V*, daily intramuscular injections of 500,000 units of vitamin A in corn oil were given him. *PA* indicates plasma vitamin A concentration in U.S.P. units per cubic centimeter, *PC* indicates plasma carotenoids concentration in equivalent U.S.P. vitamin A units, while *PB* indicates plasma bilirubin concentration in milligrams per 100 c.c. Hepatic vitamin A concentration in the sample biopsied at operation equaled 1,500 U.S.P. units per gram.

In the present study an effort was made to determine the relationship, if any, between plasma vitamin A and carotenoids concentrations, and concentration of vitamin A in hepatic tissue removed by biopsy during surgical operation. The effects of administering vitamin A intramuscularly and of giving carotene and deoxycholeic acid orally to patients with obstructive jaundice were observed, in relation to surgical release of biliary obstruction and subsidence of jaundice.

METHODS

Of the various modifications of the Carr-Price antimony trichloride reaction for the determination of vitamin A and carotene in the plasma, the method as described by McCoord and Luce-Clausen was used.[12] Vitamin A values are expressed in U.S.P. units per cubic centimeter, while plasma carotenoids values are given as U.S.P. units of equivalent vitamin A. Vitamin A concentration in the biopsied liver tissue was measured by Moore's technique.[11] Hepatic biopsy was performed at

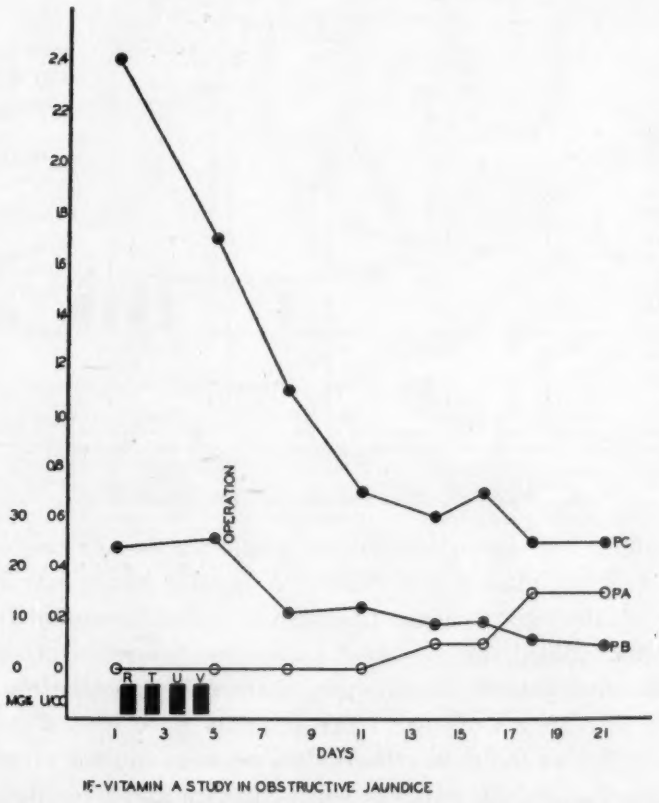


Fig. 2.—I. F., a 65-year-old woman with stones in the gall bladder and common duct and severe jaundice, had cholecystectomy and choledochostomy performed under ether anesthesia; jaundice cleared gradually after operation. Vitamin A, 500,000 U.S.P. units, was given intramuscularly at points *R*, *T*, *U*, and *V*. *PA* indicates plasma vitamin A concentration in U.S.P. units per cubic centimeter, *PC* indicates plasma carotenoids concentration expressed as U.S.P. vitamin A units per cubic centimeter, while *PB* equals plasma bilirubin concentration in milligrams per 100 c.c. Hepatic tissue biopsied at operation contained 91 U.S.P. units of vitamin A per gram.

operation by taking a wedge-shaped piece of tissue from the anterior margin of the right lobe between hemostatic stitches. The specimens weighed from 0.5 to 1.5 Gm. and the validity of this method of sampling has been tested and described.[13] In no instance was hemorrhage or bile leakage observed in consequence of the biopsy. In some cases hepatic biopsy was performed early and again late in the course of the operation

on the biliary tract. The vitamin A preparation* given parenterally consisted of vitamin A in corn oil, and contained 500,000 U.S.P. units of vitamin A per cubic centimeter. Carotene was administered orally as beta-carotene in cottonseed oil, the material used having a potency equivalent to 7,500 U.S.P. units of vitamin A per gram.†

TABLE I

PLASMA AND HEPATIC VITAMIN A VALUES IN PATIENTS WITH CHRONIC CHOLECYSTITIS, WITH OPERATION UNDER ETHER ANESTHESIA

Vitamin A not given before operation

CASE	PLASMA		HEPATIC VITAMIN A UNITS PER GM.
	CAROTENOIDS UNITS PER C.C.	VITAMIN A UNITS PER C.C.	
L. L.	2.5	1.0	486
M. M.	2.9	1.7	109
L. M.	2.4	0.5	300
A. D.	0.9	1.1	35
P. H.	1.3	1.1	52
J. V.	1.5	1.0	33
M. S.	1.0	0.9	148
A. B.	0.8	0.6	74
E. M.	0.6	0.8	352
B. B.	1.2	1.2	417
M. S.	1.4	1.3	428
M. L.	1.0	0.2	25
I. F.	1.3	1.4	533
Average	1.5	0.98	230

PRESENTATION OF DATA, AND COMMENT

In Table I are shown values for concentration of carotenoids and vitamin A in the plasma and vitamin A in liver biopsy specimens from a group of thirteen patients undergoing cholecystectomy for chronic cholecystitis. Blood samples were taken just before induction of ether anesthesia, and hepatic biopsy was performed immediately after the peritoneal cavity was opened. The patients were without evidence of active infection at the time. These data serve as control values in interpreting the findings in patients with jaundice and liver damage. The wide range in plasma and hepatic vitamin A values is noteworthy. Dark adaptation measurements were not made in this study, and although these patients presented no symptoms or objective evidence of vitamin A lack, it is not certain that subclinical deficiency may not have been present in some instances.

In Table II are shown results of similar analyses in a group of nine patients with obstructive jaundice of high degree. No carotene or vitamin A had been given the patients preoperatively. Again, considerable fluctuation is noted in the plasma carotenoids, but in every case

*Kindly prepared by Dr. A. Black, of the Biological Laboratories of E. R. Squibb & Sons.

†Deoxycholeic acid for oral use was supplied by Riedel-de Haen, Inc.

the plasma vitamin A value was zero, and in four cases vitamin A could not be detected in the hepatic sample. These data demonstrate that in obstructive jaundice the plasma may contain no vitamin A, even though the concentration of plasma carotenoids is within normal limits, and vitamin A is present in the liver.

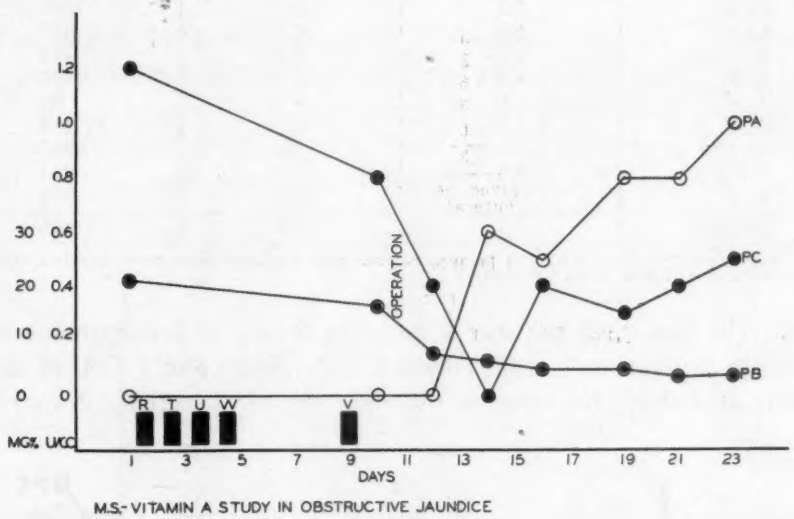


Fig. 3.—M. S., a 36-year-old man with carcinoma of the head of the pancreas, severe jaundice, and diabetes mellitus, had cholecystgastrostomy done under spinal anesthesia, after which the jaundice subsided rapidly and insulin requirements abruptly declined. At points marked *R*, *T*, *U*, *W*, and *V* daily intramuscular injections of vitamin A, 500,000 U.S.P. units each, were given. *PA* indicates plasma vitamin A concentration in U.S.P. units per cubic centimeter, *PC* indicates plasma carotenoids concentration expressed as U.S.P. units of vitamin A per cubic centimeter, while *PB* indicates plasma bilirubin concentration in milligrams per 100 c.c. Vitamin A concentration in hepatic biopsy sample taken at operation was 353 U.S.P. units per gram.

TABLE II

PLASMA AND HEPATIC VITAMIN A VALUES IN PATIENTS WITH OBSTRUCTIVE JAUNDICE NOT RECEIVING VITAMIN A BEFORE OPERATION

CASE	PLASMA		HEPATIC VITAMIN A UNITS PER GM.
	CAROTENOIDS UNITS PER C.C.	VITAMIN A UNITS PER C.C.	
F. D.	1.1	0	57
F. H.	3.2	0	0
M. B.	1.9	0	79
J. S.	2.3	0	56
M. C.	0.4	0	0
M. K.	1.9	0	307
B. D.	1.6	0	312
E. Z.			0
E. B.	0.6	0	0
Average	1.6	0	90

By contrast, Table III presents the data from patients who had received large doses of vitamin A or carotene before operation. The first eight patients in the table received 500,000 U.S.P. units of vitamin A intramuscularly daily for three or four days immediately before opera-

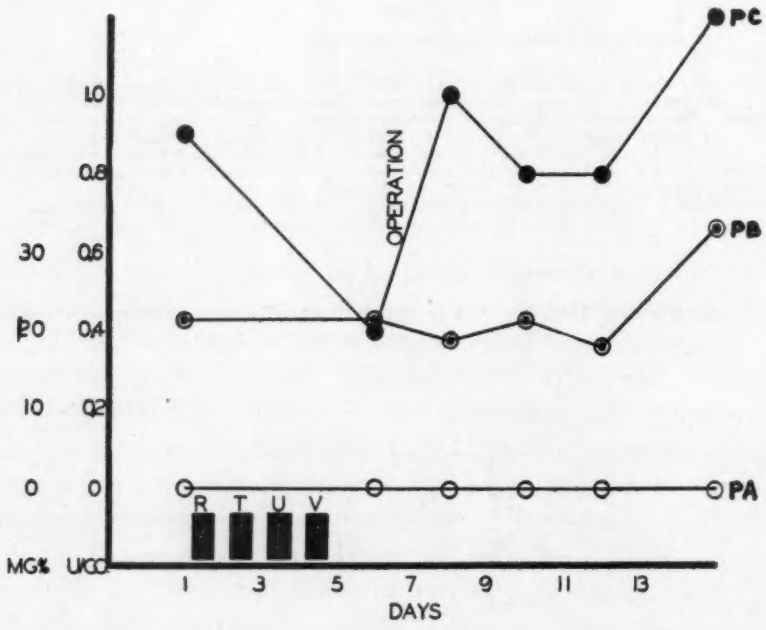
TABLE III

PLASMA AND HEPATIC VITAMIN A VALUES IN PATIENTS WITH OBSTRUCTIVE JAUNDICE

CASE	PLASMA		HEPATIC VITAMIN A UNITS PER GM.
	CAROTENOIDS UNITS PER C.C.	VITAMIN A UNITS PER C.C.	
F. H.	1.0	0	688
E. S.	0.8	0.5	750
P. R.	1.1	0	1500
L. C.	0.4	0	136
M. S.	0.8	0	353
I. F.	1.7	0	91
A.. S.	0.5	0	50
J. C.	1.2	0.2	115
R. M.*	3.6	0.9	417
W. W.*	2.5	1.2	344
L. B.*	0.6	0.5	118
Average	1.3	0.3	413

*These patients had received beta-carotene and deoxycholeic acid orally; the rest had received vitamin A parenterally.

tion. The last three patients were given 8 Gm. of beta-carotene in oil (vitamin A equivalent total 60,000 U.S.P. units) and 1 Gm. of deoxycholeic acid daily for three to five days before operation. No striking



L.C.- VITAMIN A STUDY IN OBSTRUCTIVE JAUNDICE

Fig. 4.—L. C., a 59-year-old woman with gallstones and inoperable carcinoma of the hepatic ducts and liver, jaundice not relieved by operation under ether anesthesia, died of liver failure and pneumonia ten days after operation. At points *R*, *T*, *U*, and *V* vitamin A was injected intramuscularly in doses of 500,000 U.S.P. units daily. *PC* indicates plasma carotenoids concentration expressed as U.S.P. units of vitamin A per cubic centimeter, *PA* indicates plasma vitamin A concentration in U.S.P. units per cubic centimeter, and *PB* indicates plasma bilirubin concentration in milligrams per 100 c.c. Concentration of vitamin A in hepatic tissue biopsied at operation was 136 U.S.P. units per gram.

effect on plasma values of carotenoids and vitamin A is seen as a result of such treatment. However, though much variation in hepatic vitamin A content is evident, hepatic storage of the vitamin is clearly visible. As shown in case P. R., under these conditions very high concentration of vitamin A may be present in the liver while the plasma concentration is still zero.

The data of Table IV suggest two conclusions. Lengthy operation on the biliary tract under ether anesthesia apparently produces little or no change in hepatic vitamin A concentration. Furthermore, the validity of the sampling method is supported by the finding of similar vitamin A values in the specimens taken at the beginning, and again at the end, of the operation.

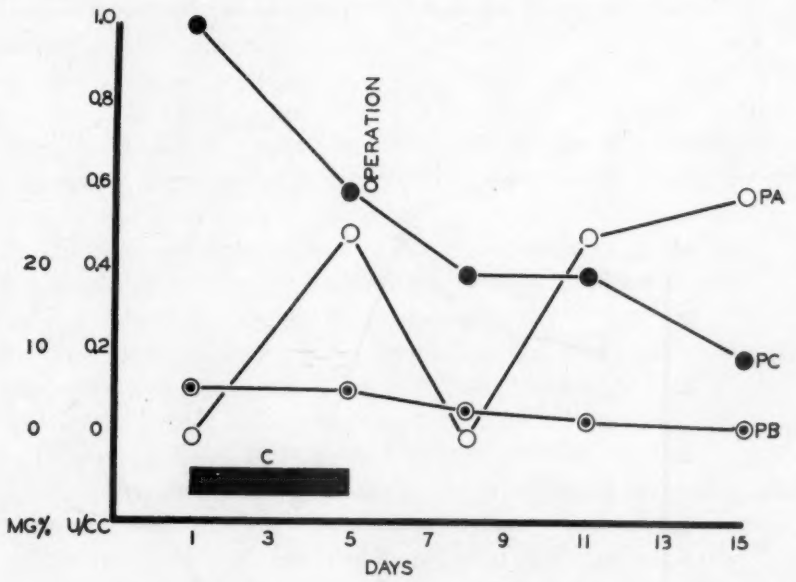


Fig. 5.—L. B., an obese, elderly, mildly jaundiced woman was found to have a stone impacted at the papilla of Vater, which was removed under ether anesthesia by choledochostomy and duodenotomy. Before operation during the period marked *C*, 8 Gm. of carotene in cottonseed oil and 1 Gm. of deoxycholeic acid were given orally each day, the vitamin A equivalent per day being 60,000 U.S.P. units. *PA* indica es plasma vitamin A concentration in U.S.P. units per cubic centimeter, *PC* indicates plasma carotenoids concentration expressed as U.S.P. units of vitamin A per cubic centimeter, and *PB* indicates plasma bilirubin concentration in milligrams per 100 c.c. Vitamin A concentration in hepatic tissue biopsied at operation was 118 U.S.P. units per gram.

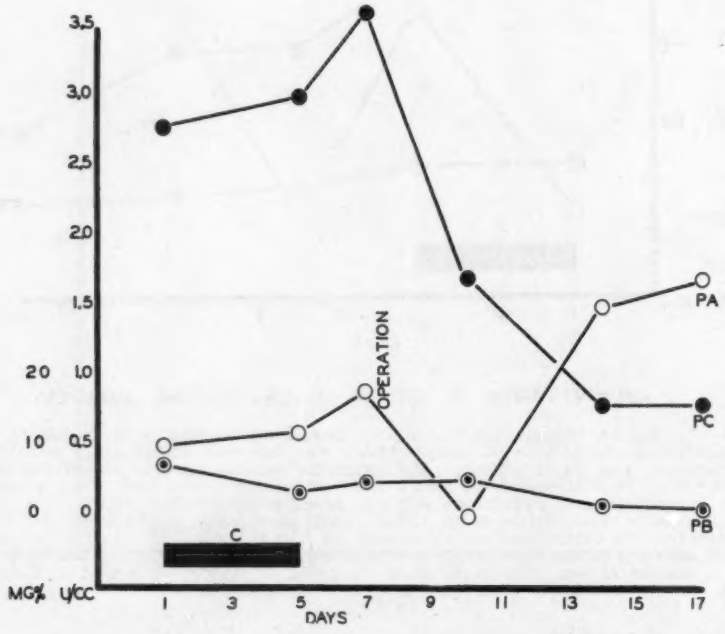
In Figs. 1, 2, 3, 4, 5, and 6 are shown values for concentration of vitamin A, carotenoids, and bilirubin in the plasma, before and after operation. Vitamin A, or carotene, was administered before operation. In one patient, as shown in Fig. 3, inoperable obstruction to the hepatic ducts was encountered and death resulted from liver failure and pneumonia ten days after operation. In this case the plasma vitamin A value remained zero despite the fact that a total of 2,000,000 U.S.P. units had

been administered intramuscularly before operation. Since the biopsied hepatic tissue at operation contained vitamin A, the findings in this case suggest that plasma vitamin A concentration may be decreased as a result of impaired liver function, regardless of the presence of vitamin A in the liver. The data shown graphically in Fig. 1 offer further support to this conception, for despite the extremely high vitamin A content of the liver at operation, that is, 1,500 units per gram, never-

TABLE IV

EFFECT OF OPERATION AND ETHER ANESTHESIA ON HEPATIC VITAMIN A CONCENTRATION IN OBSTRUCTIVE JAUNDICE

CASE	INITIAL HEPATIC VITAMIN A UNITS PER GM.	FINAL HEPATIC VITAMIN A UNITS PER GM.	DURATION OF OPERATION IN MINUTES
A. S.	50	50	80
J. C.	115	125	70
W. W.	334	278	50
M. K.	307	312	75
B. D.	271	250	140
I. F.	91	68	140



R.M.- VITAMIN A STUDY IN OBSTRUCTIVE JAUNDICE

Fig. 1.—R. M., a 57-year-old man with stones in the gall bladder and common duct and mild jaundice had cholecystectomy and choledochostomy performed under ether anesthesia, followed by uneventful convalescence. During the period marked *C*, 8 Gm. of carotene in cottonseed oil and 1 Gm. of deoxycholeic acid were given orally each day, the vitamin A equivalent per day being 60,000 U.S.P. units. *PA* indicates plasma vitamin A concentration in U.S.P. units per cubic centimeter, *PC* indicates plasma carotenoids concentration expressed as U.S.P. units of vitamin A per cubic centimeter, and *PB* indicates plasma bilirubin concentration in milligrams per 100 c.c. Vitamin A concentration in hepatic tissue biopsied at operation was 417 U.S.P. units per gram.

theless the plasma value returned to normal only with subsidence of jaundice postoperatively, and improvement in liver function.

In two patients, L. B. as shown in Fig. 5, and R. M. as shown in Fig. 6, plasma vitamin A was reduced at the time of operation but not entirely absent, and it is of interest that further decrease occurred immediately after operation. This event suggests the parallel finding of postoperative decrease in plasma prothrombin in patients with obstructive jaundice[14] and supplies further evidence of the importance of hepatic function in the regulation of plasma vitamin A level.

The data appearing in the illustrations demonstrate that concentrations of plasma vitamin A and plasma carotenoids tend to vary inversely, a point which is particularly well shown in Fig. 1. Vitamin A and carotene were not given the patients postoperatively, and the decline in plasma carotenoids possibly depends on more rapid conversion of the provitamin with improvement in liver function.

SUMMARY

Concentrations of vitamin A and carotenoids in the plasma, and concentration of vitamin A in biopsied liver samples have been determined in the following groups of patients:

1. Thirteen patients undergoing cholecystectomy for chronic cholecystitis and cholelithiasis, without jaundice or evidence of active infection, and not given vitamin A preoperatively.

2. Nine patients undergoing operation for obstructive jaundice of high degree and not given vitamin A preoperatively.

3. Eight patients undergoing operation for obstructive jaundice after receiving large doses of vitamin A parenterally.

4. Three patients operated upon for obstructive jaundice after receiving carotene and deoxycholeic acid orally.

In six patients the liver was biopsied at the beginning and again at the end of operation on the biliary tree under ether anesthesia.

Plasma concentrations of vitamin A, carotenoids, and bilirubin were repeatedly determined before and after operation and are presented graphically from five cases in which biliary obstruction was relieved by operation, and in one case of inoperable carcinoma of the hepatic ducts.

CONCLUSIONS

1. Concentrations of vitamin A and carotenoids in the plasma, and concentrations of vitamin A in the liver vary considerably in patients with chronic cholecystitis, but a rough correlation between plasma and hepatic vitamin A content is evident.

2. In patients with obstructive jaundice not given vitamin A, plasma vitamin A values of zero are common, though plasma concentrations of carotenoids may be normal. Vitamin A values in biopsied liver tissue likewise may be zero.

3. Administration of large amounts of vitamin A parenterally, or carotene and deoxycholeic acid orally before operation in patients with obstructive jaundice is followed by the finding of normal vitamin A values in the biopsied liver specimen; rise in plasma vitamin A concentration, however, occurs more slowly, and may depend on improvement in liver function as produced by release of biliary obstruction.

4. Hepatic vitamin A concentration does not appear to change significantly during the course of operations on the biliary tract under ether anesthesia; postoperative reduction in plasma vitamin A concentration, however, is to be expected.

REFERENCES

1. Bessey, O. A., and Wolbach, S. B.: Vitamin A.: Physiology and Pathology. The Vitamins, Chicago, 1939, American Medical Association.
2. Greaves, J. D., and Schmidt, C. L. A.: On the Absorption and Utilization of Carotene and Vitamin A in Choledochocolonostomized Vitamin A Deficient Rats, Am. J. Physiol. **111**: 492, 1935.
3. Altschule, M. D.: Vitamin A Deficiency in Spite of Adequate Diet in Congenital Atresia of Bile Ducts and Jaundice, Arch. Path. **20**: 845, 1935.
4. Baumann, C. A., Riising, B. M., and Steenbock, H.: The Absorption and Storage of Vitamin A in the Rat, J. Biol. Chem. **107**: 705, 1934.
5. May, C. D., Blackfan, K. D., McCreary, J. F., and Allen, F. H., Jr.: Clinical Studies of Vitamin A in Infants and in Children, Am. J. Dis. Child. **59**: 1167, 1940.
6. Steininger, G., Roberts, L. J., and Brenner, S.: Vitamin A in the blood of Normal Adults: The Affect of a Depletion Diet on Blood Values and Biophotometer Readings, J. A. M. A. **113**: 2381, 1939.
7. Abels, J. C., Gorham, A. T., Pack, G. T., and Rhoads, C. P.: Metabolic Studies in Patients With Cancer of the Gastrointestinal Tract. I. Plasma Vitamin A Levels in Patients With Malignant Neoplastic Disease, Particularly of the Gastrointestinal Tract, J. Clin. Investigation **20**: 749, 1941.
8. Crimm and Short: Quoted by Ralli, Papper, Paley, and Baumann.
9. Ralli, E. P., Papper, E., Paley, K., and Baumann, E.: Vitamin A and Carotene Content of Human Liver in Normal and in Diseased Subjects: An Analysis of 116 Human Livers, Arch. Int. Med. **68**: 102, 1941.
10. Fox, F. W.: Vitamin A in the Livers of Native Mine Workers With Special Reference to Their Resistance to Pneumonia, Lancet **1**: 953, 1933.
11. Moore, T.: Vitamin A and Carotene: the Vitamin A Reserve of the Adult Human Being in Health and Disease, Biochem. J. **31**: 155, 1937.
12. McCoord, A. B., and Luce-Clausen, Ethel, M.: The Storage of Vitamin A in the Liver of the Rat, J. Nutrition **7**: 557, 1934.
13. Rourke, G. M., and Stewart, J. D.: On the Uniformity of Hepatic Composition With Respect to Concentration of Certain Biochemical Constituents in Different Parts of the Same Liver, Arch. Path. In press.
14. Stewart, J. D.: Prothrombin Deficiency and the Effects of Vitamin K in Obstructive Jaundice and Biliary Fistula, Ann. Surg. **109**: 588, 1939.

THE VALUE OF SKIN RESISTANCE STUDIES IN DETERMINING THE ACCURACY OF PROCAINE INJECTIONS OF THE SYMPATHETIC NERVES

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PROCAINE injection of the sympathetic nerves has become an invaluable aid in the study of the peripheral circulation and in the treatment of certain vascular disorders. These injections are made after the skin temperature of the affected limb has become stabilized through exposure to cold. If following the attempted sympathetic block there occurs a substantial increase in the skin temperature of the affected limb, not only is a significant element of vasospasm and a good capacity of the vascular bed for dilatation demonstrated, but the efficacy of the procaine injection is proved. If, on the other hand, little or no elevation in skin temperature takes place, the question always arises as to whether the circulatory difficulty is entirely due to obliterative arterial disease with no significant element of vascular spasm, or whether the operator has failed to achieve a satisfactory anesthesia. In the study of the upper extremities this question may be settled by the presence of a Horner's syndrome, but there is no similarly helpful sign in the study of the lower extremities, in which almost all the cases of severe obliterative arterial disease occur. There are, furthermore, occasions for therapeutic procaine injection or for procaine block preliminary to alcohol injection when it is either not necessary or perhaps even undesirable to expose the affected part to a cold room temperature. It is apparent that any method which might help in determining the accuracy of sympathetic injections would be a useful adjunct.

It has been known for some time that the resistance of the skin to passage of a small electric current is very high in areas in which sympathetic denervation has been brought about by operation.[1] Dr. C. P. Richter has been very helpful in outlining the denervated area in most of the patients whom I have subjected to sympathectomy, and a definite correlation has been found between the area of high skin resistance and the level and extent of the operative procedure.[1] Similar changes are present after chemical section of the sympathetics by means of alcohol injection. It occurred to me that the same changes would probably be present during the period of sympathetic anesthesia following procaine injection and that these studies would be helpful in determining whether an injection resulted in successful sympathetic paralysis.

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METHOD AND EXPERIMENTAL OBSERVATIONS

The limbs to be studied were exposed in a cool room, generally about 20° C., until the skin temperature had become stable. During this period a number of observations of cutaneous resistance were made with a machine similar to that described by Levine.[1, 2] This machine permits one to measure the current passed through the skin and the number of ohms resistance offered by the skin to passage of the current. A zinc electrode covered with kaolin paste is fixed to the lobe of one ear at a site where the skin has been punctured with a needle. The other zinc electrode is applied to the skin of the limbs being studied. The operator becomes adept in holding the electrode against the skin with approximately the same amount of pressure and for approximately the same interval of time during each reading. The potentiometer knobs are turned until the galvanometer which serves as an ammeter registers passage of exactly two microamperes. The other galvanometer, which is used as a voltmeter and which measures the voltage necessary to send through this amperage, is calibrated so that the number of ohms resistance can be read directly. Accurate observations of skin resistance can be made up to 3,800,000 or 4,000,000 ohms. Higher values cannot be read accurately and in the records and figures are recorded as too high to be read (T. H.). At least one point on the dorsum and one on the palm or sole were selected for reading in each patient, the points being the same on both hands or both feet. These sites for resistance readings were selected where the resistance was not high, and in order to obviate inadvertent change in the point of reading, each was marked with a skin pencil. Generally the needles through which the procaine was injected were left in place until the skin resistance in the ipsilateral hand or foot had begun to increase substantially, indicating that an effectual block was being accomplished.

Studies were made upon twenty-one subjects. These were patients with various types of peripheral vascular disorders: Raynaud's disease, Raynaud's disease and arthritis, Buerger's disease associated with varying degrees of vasospasm, peripheral arteriosclerosis with and without accompanying vascular spasm, acute thrombophlebitis, thrombophlebitic sequelae, traumatic reflex edema and causalgia, and vasospasm and calcinosis. Four patients subjected to upper dorsal sympathetic blocks, sixteen to lumbar sympathetic blocks, and one to spinal anesthesia were studied. In Table I are recorded the skin resistance values before injection and at a time after injection when the difference between the two limbs was maximal. In every instance the study of cutaneous resistance was helpful in determining whether the injection produced satisfactory anesthesia. All injections except one were successful and were accompanied by marked rise in skin resistance on the side on which the injection was made. In one case (Case 19) the operator was unsuccessful in

obtaining sympathetic anesthesia, as evidenced by failure to obtain a rise in skin temperature after the injection, and subsequent demonstration of a fairly good capacity of the vascular bed for vasodilatation by other observations, including operative sympathectomy. This failure of sympathetic anesthesia was obvious because there was not the characteristic unilateral increase in cutaneous resistance which was observed in

TABLE I

CUTANEOUS RESISTANCE BEFORE AND AFTER ATTEMPTED SYMPATHETIC ANESTHESIA

NO.	NAME	CUTANEOUS RESISTANCE IN OHMS					TYPE OF INJECTION
		POINT	BEFORE INJECTION		AFTER INJECTION		
			RIGHT	LEFT	RIGHT	LEFT	
1	E. M.	Dorsum	1,500,000	2,800,000	1,000,000	T.H.	Left dorsal
		Palm	350,000	900,000	220,000	T.H.	
2	M. M.	Dorsum	350,000	330,000	1,900,000	210,000	Right dorsal
		Palm	100,000	540,000	T.H.	500,000	
3	M. B.	Dorsum	160,000	150,000	130,000	500,000	Left dorsal
		Palm	T.H.	T.H.	270,000	3,350,000	
4	C. B.	Dorsum	T.H.	T.H.	T.H.	T.H.	Right dorsal
		Palm	100,000	140,000	T.H.	400,000	
5	C. F.	Dorsum	350,000	700,000	950,000	T.H.	Left lumbar
		Sole	300,000	190,000	200,000	1,000,000	
6	D. F.	Dorsum	390,000	570,000	290,000	T.H.	Left lumbar
		Sole	1,300,000	1,200,000	1,100,000	T.H.	
7	I. R.	Dorsum	3,500,000	3,100,000	T.H.	200,000	Right lumbar
		Sole	600,000	300,000	T.H.	300,000	
8	F. N.	Dorsum	700,000	500,000	1,400,000	T.H.	Left lumbar
9	S. G.	Dorsum	390,000	300,000	T.H.	310,000	Right lumbar
		Sole	410,000	510,000	T.H.	390,000	
10	I. R.	Dorsum	720,000	330,000	T.H.	460,000	Right lumbar
		Sole	1,700,000	1,500,000	650,000	460,000	
11	C. B.	Dorsum	300,000	250,000	530,000	T.H.	Left lumbar
		Sole	500,000	980,000	690,000	T.H.	
12	G. C.	Dorsum	2,400,000	1,600,000	T.H.	1,450,000	Right lumbar
		Sole	2,700,000	1,750,000	T.H.	1,200,000	
13	R. B.	Dorsum	890,000	950,000	T.H.	1,000,000	Right lumbar
		Sole	600,000	500,000	T.H.	400,000	
14	R. M.	Dorsum	520,000	500,000	540,000	1,100,000	Left lumbar
		Sole	890,000	520,000	890,000	2,100,000	
15	L. S.	Dorsum	790,000	900,000	T.H.	1,950,000	Right lumbar
		Sole	3,000,000	2,800,000	T.H.	2,100,000	
16	F. C.	Dorsum	1,700,000	1,200,000	T.H.	2,000,000	Right lumbar
		Sole	600,000	500,000	3,250,000	480,000	
17	P. E.	Dorsum	1,100,000	400,000	1,600,000	T.H.	Left lumbar
		Sole	T.H.	450,000	T.H.	2,000,000	
18	M. H.	Dorsum			1,300,000	T.H.	Left lumbar
		Sole			2,000,000	T.H.	
19	F. D.	Dorsum	160,000	160,000	1,400,000	600,000	Left lumbar
		Sole	580,000	600,000	T.H.	1,650,000	
20	T. S.	Dorsum	T.H.	T.H.	T.H.	T.H.	Left lumbar
		Sole	T.H.	T.H.	T.H.	T.H.	
		Leg*	1,500,000	1,000,000	1,000,000	T.H.	
21	R. C.	Dorsum	191,000	430,000	2,900,000	T.H.	Spinal (Pontocaine 10 mg.)
		Sole	750,000	490,000	T.H.	T.H.	

*These readings were made with kaolin paste on the electrode.

all other instances. In each patient subjected to a dorsal block distinct Horner's syndrome occurred as well as prompt and significant rise in both skin resistance and skin temperature.

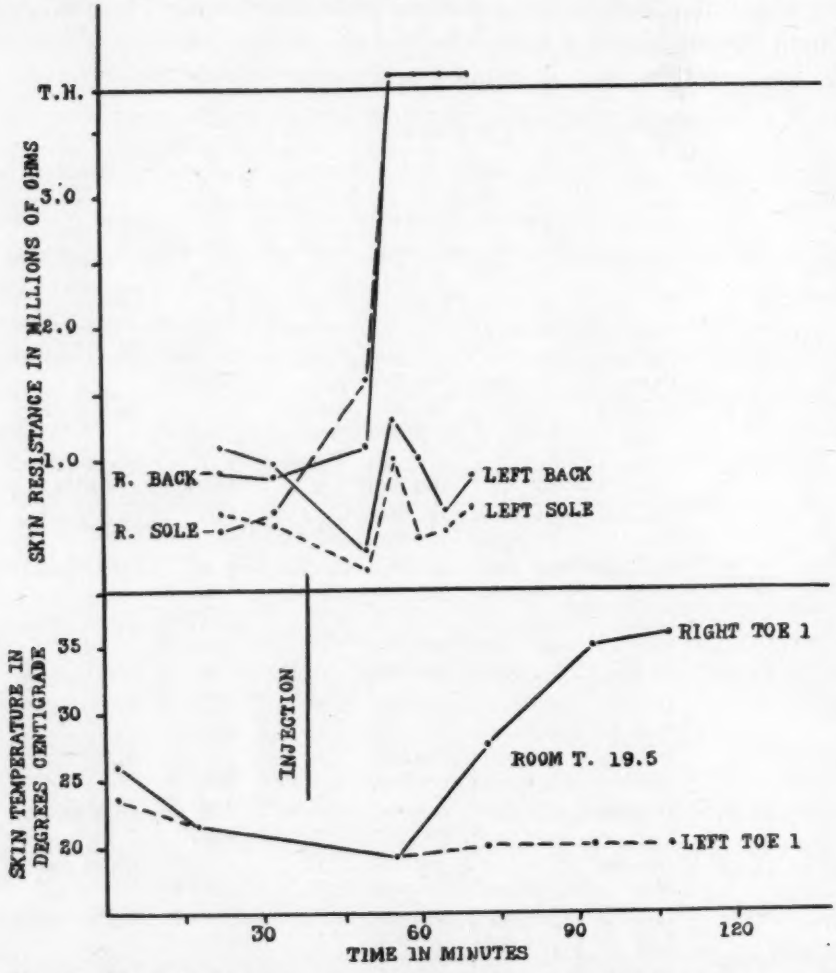

Fig. 1.—Chart showing rise in skin resistance and skin temperature in the ipsilateral foot following right lumbar sympathetic block (Case 13). Postphlebitic ulceration, edema, and vasospasm.

In Figs. 1 and 2 are charted the changes in skin resistance and in skin temperature in two patients who showed the customary increase in skin resistance following procaine block of the lumbar sympathetics and who also responded with increased warmth in the foot.* One was a patient with postphlebitic edema, ulceration, and vasospasm, the other a patient with peripheral arteriosclerosis and peripheral neuritis. In

*In these and in the other cases charted, changes in the temperature of only a single digit on each side are recorded, for the sake of simplicity. In all cases, however, several digits of each hand or foot are always studied. In addition I always record temperature changes on the soles of the feet. I feel that such multiple readings are very important. Sometimes there will be no rise in temperature of the great toe whereas there will be an excellent response in the other toes and the sole. If only the great toe were studied one might conclude that no improvement could be expected from sympathectomy when as a matter of fact decided improvement could be anticipated.

Fig. 3 is shown for comparison a chart of the changes in skin temperature and skin resistance after spinal anesthesia in a young man with recurrent migrating phlebitis and vasospasm. In all three instances the rise in skin temperature of the ipsilateral foot was adequate evidence of the efficacy of the sympathetic injection. In Fig. 4, however, the record is charted of a patient in whom it would have been impossible without the skin resistance studies to know whether a good sympathetic block had been obtained. The failure of the skin temperature to rise

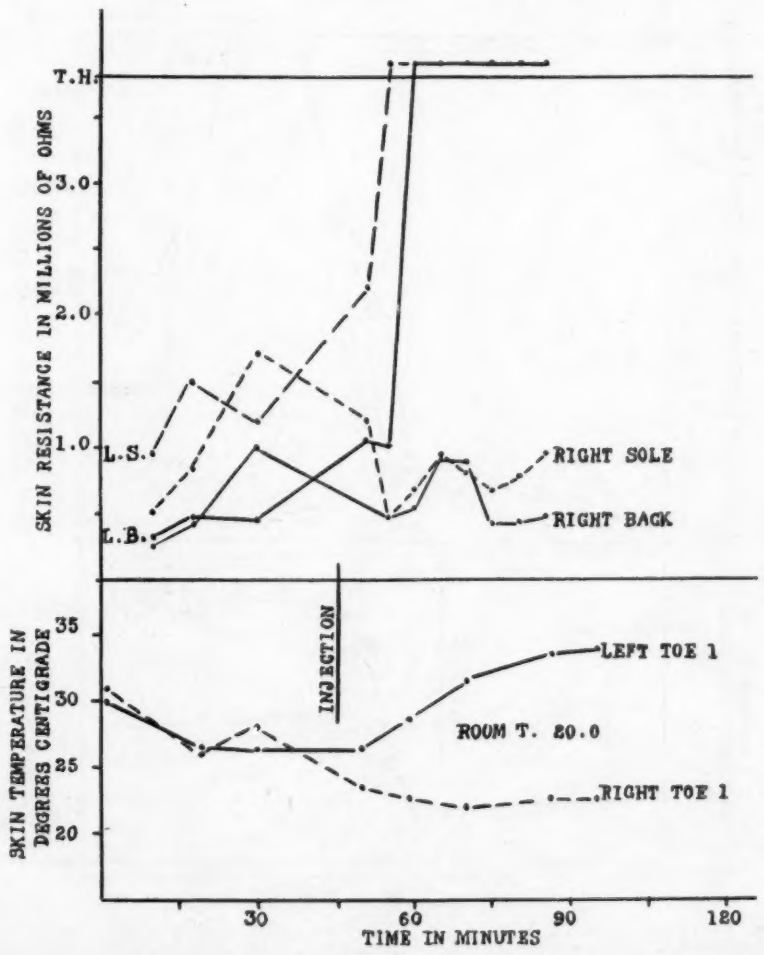

Fig. 2.—Chart showing rise in skin resistance and skin temperature in the ipsilateral foot following left lumbar sympathetic block. Case 11. Peripheral arteriosclerosis and peripheral neuritis.

significantly might have been due to the inability of the vascular bed to dilate, or it might have been due to failure in producing successful sympathetic paralysis. The prompt increase in skin resistance on the injected side gave convincing proof that the former was the case. In this series there were a number of other instances in which little or no rise

in skin temperature occurred and in which, without the resistance studies, one would have wondered whether the sympathetic block had been completely or partly ineffectual.

The resistance of the normally innervated skin is lowest when the patient has been warmed by exposure of the body in a hot-air cabinet and when sweating is active; it is much higher when the body is cold. For this reason the skin resistance studies which are carried out on

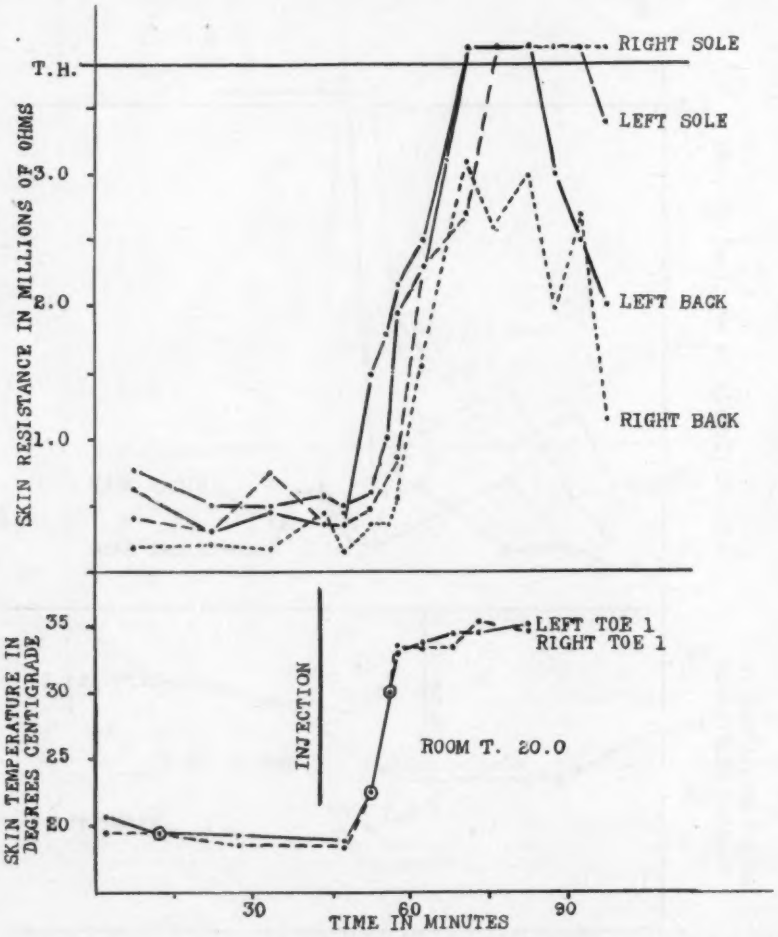

Fig. 3.—Chart showing rise in skin resistance and skin temperature in the foot following spinal anesthesia (10 mg. pontocaine). Case 21. Migrating phlebitis and vasospasm.

sympathectomized patients have been done immediately after the patient has been heated in a cabinet. With such preparation any abnormally high skin resistance is more significant and the affected area can be more sharply outlined because the resistance in the normally innervated areas is so low. When the present investigation was begun this matter afforded me some concern, for I was not sure whether the skin resistance in a patient exposed to cold would be sufficiently low to permit a clear-cut

demonstration of the unilateral increase following effectual sympathetic block. Generally the initial skin resistance in both feet or both hands, and the final values on the uninjected side were relatively low compared with the very high values present after sympathetic anesthesia was obtained. Occasionally the values were rather high, as in Cases 12 and 15, but still the differences after sympathetic injection were striking. Sometimes when the initial values were rather high, as in Case 7, as the

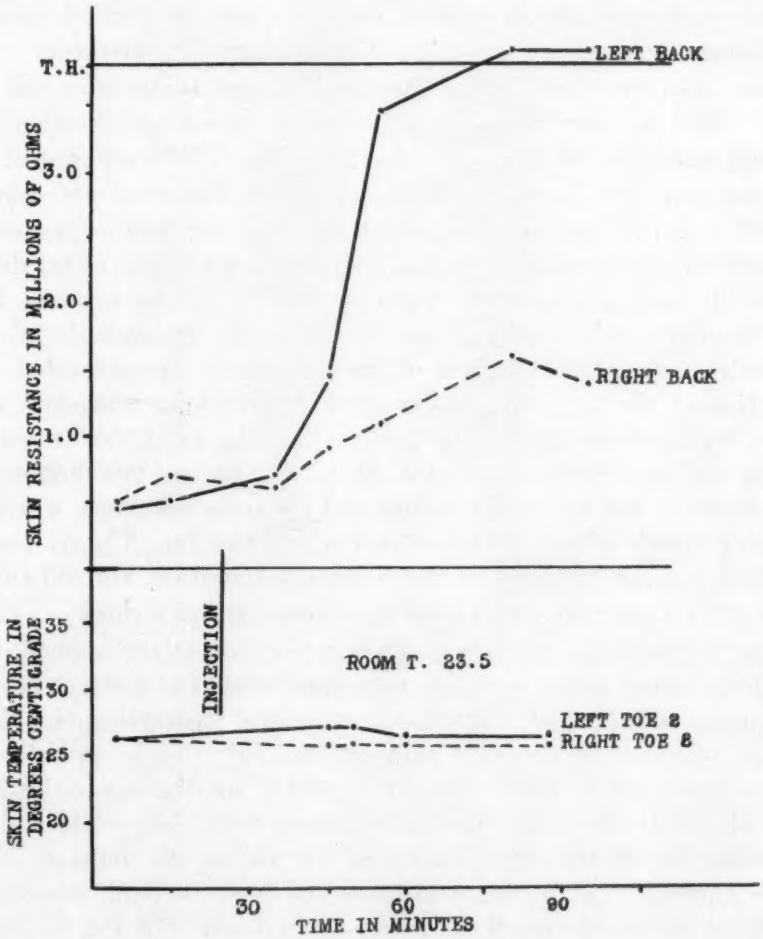

Fig. 4.—Chart showing rise in skin resistance in the ipsilateral foot following left lumbar sympathetic block in a patient in whom there was no increase in skin temperature. Case 8. Diabetes, arteriosclerosis, gangrene of toe.

study progressed the skin resistance in the unanesthetized limb fell in such a way as to make the differences very great. In Case 17 the skin resistance remained rather high on the back of the right foot and too high to read on the right sole. The low skin resistance on the left foot, however, gave way to very high values after left lumbar sympathetic block was accomplished, and there was no difficulty in interpreting the

resistance studies as indicative of an effectual block. During the sympathetic anesthesia in this case the dorsum of each foot was explored extensively with the electrode. Only one point was found on the left foot where the skin resistance was low enough to permit one to obtain a reading, whereas the values on the unanesthetized right dorsum were everywhere low enough for reading. In Case 4 the resistance of the dorsal surface of both hands was too high to be read, but study of the resistance of the palms gave adequate information. Similarly in Case 8, the skin resistance on the soles of both feet was too high to read, but satisfactory information could be derived from measurements on the dorsum (Fig. 4). Only in one instance did high values offer real difficulty. This was the case of a patient with severe peripheral arteriosclerosis and diabetic neuritis (Case 20). The skin resistance of both feet was too high to read. Although my studies were not complete enough to permit me to be certain, I feel that this was an instance of sympathetic denervation which had occurred in the course of her disease, similar to cases which I have reported.[3] Even in this instance I was able to obtain confirmation of the efficacy of the sympathetic injection by studying the skin resistance of the legs, which was somewhat lower than that of the feet, with kaolin on the electrode, a procedure which lowers the readings. After injection the reading was 1,000,000 ohms on one leg and too high to read on the other. The patient was then warmed with blankets and hot water bottles and the same difference was found where one used the plain zinc electrode without kaolin. The sympathetic injection was not attended by rise in skin temperature, nor did any rise occur after a posterior tibial block was carried out as a check.

Case 18 illustrates another possible application of the method. This patient, who had severe peripheral arteriosclerosis and a recent popliteal thrombosis, was studied without skin resistance measurements. No rise in skin temperature followed paravertebral injection of procaine, and it was important to know whether a good sympathetic anesthesia had been obtained. Readings of skin resistance were then made and they confirmed the efficacy of the block. In this patient one could outline the entire extremity as having resistance too high to read, whereas the values on the contralateral limb were much lower. In Fig. 5 this contrast is shown. The area of high skin resistance is of the same extent as that found following first, second, and third lumbar ganglionectomy.[1] Injections of procaine had been made at the level of the first and second ganglia. In a number of other cases the area of sympathetic anesthesia could be outlined similarly, but not infrequently the readings on the thighs were too high to permit sharp outlining of the extent of anesthesia. Undoubtedly one could do so if he were to warm the patient sufficiently before the anesthesia had worn off and if the result should ever appear doubtful, I should follow this procedure.

It has been my feeling that the more accurately the tips of the needles are placed in close proximity to the sympathetic ganglia, the quicker the occurrence of the rise in skin temperature in the hand or foot, and I believe that in general this is the correct explanation. Occasionally, however, the rise in skin temperature is extremely tardy* and such occur-

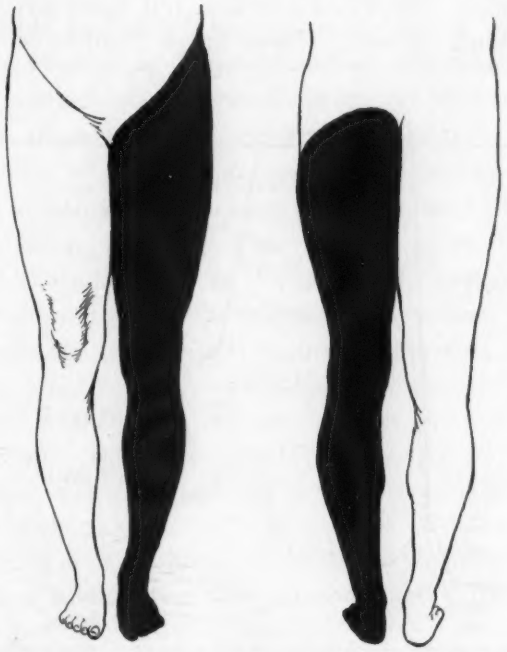

Fig. 5.—Showing the area of high skin resistance in the ipsilateral extremity following left lumbar sympathetic block. The shaded area represents the area in which the skin resistance was too high to read. Case 18. Arteriosclerosis, left popliteal thrombosis.

rences have been very puzzling to me. Case 9, which is charted in Fig. 6, is an interesting example. It will be seen from the rapid and significant rise in cutaneous resistance that the sympathetic injection was made accurately and that prompt anesthesia resulted. It was almost an hour, however, before any rise in skin temperature occurred. Once this began the temperature rose rapidly to a normal level. Operative sympathectomy was similarly followed by great increase in warmth. Why there should be such a long delay in the rise in temperature of the foot after effective sympathetic anesthesia I cannot say. It is hoped that additional observations of similar reactions may throw some light upon this interesting problem. It should be noted that there is generally a lag of some minutes in the beginning of rise in skin temperature after the skin resistance has begun to increase, as is to be expected since increased heat is an effect of vasodilatation and not an instantaneous reaction.

*For this reason I always make observations of temperature for at least an hour after injection, even when no increase occurs.

DISCUSSION

Diminished peripheral arterial circulation may be due to occlusion of vessels, to vasospasm, or to a combination of the two. The determination of the category in which each case belongs and the degree of vasospasm present is not only helpful in sorting out the peripheral vascular diseases but is essential to their rational treatment. There is no way of restoring blood flow through obliterated arteries, but there are effective means of releasing vascular spasm. There are a number of useful tests for

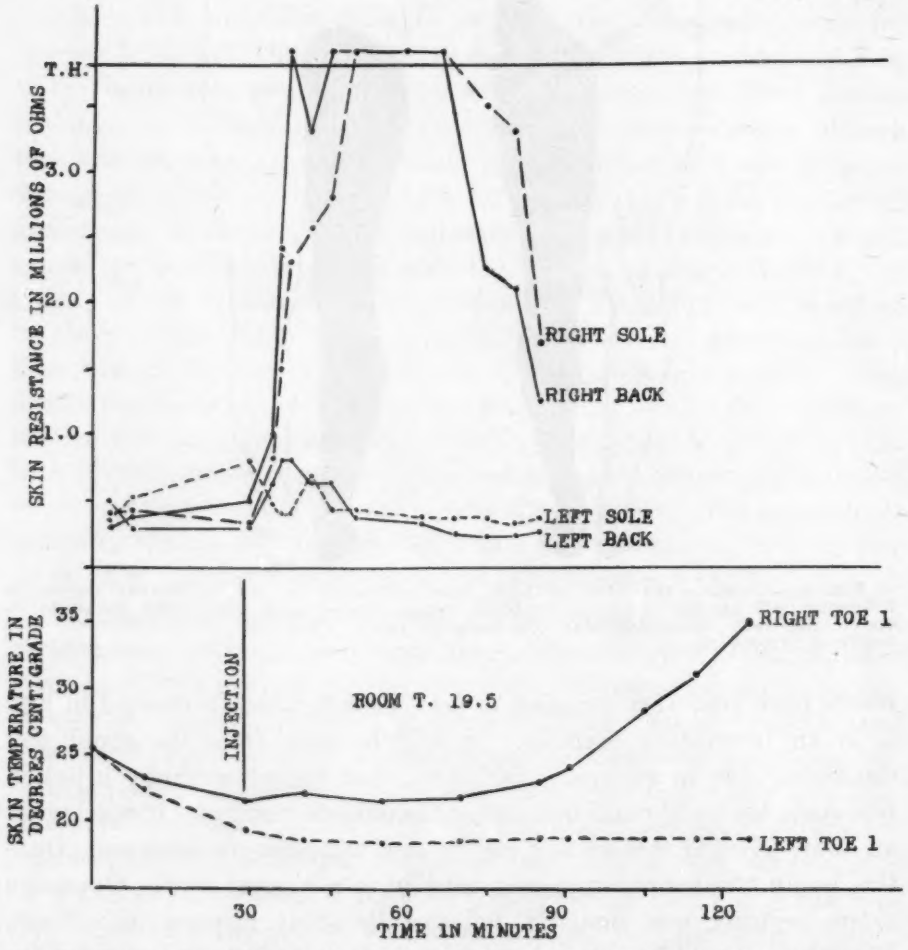

Fig. 6.—Showing prompt rise in skin resistance and delayed rise in skin temperature following right lumbar sympathetic block in Case 9. Buerger's disease.

inhibiting sympathetic vasoconstrictor impulses, depending either upon release of vascular tone in some indirect manner or upon interruption of sympathetic impulses by anesthesia. The effect is usually noted by observation of changes in skin temperature. These observations may be supplemented by digital plethysmography, oscillometry, or plethysmographic blood flow studies.

The artificial fever of typhoid vaccination[4] is no longer employed as a test since more satisfactory methods have replaced it. The observation of temperature changes in cooled extremities when the body is warmed by a hot-air cabinet,[5] by wrapping in blankets and rubber sheet,[6] by electric pads, or by diathermy over the lumbosacral area[7] is a simple and helpful test. Similarly useful is the immersing of the other extremities in warm water.[8] I sometimes use such body-heating tests, especially when it is desirable to study vascular spasm both in upper and lower extremities at the same time. If good vasodilatation does not occur, however, I feel that it is necessary to check the matter by direct sympathetic injection or some other test. General anesthesia can be used to demonstrate the presence or absence of vasospasm[9] but is not ordinarily advisable unless anesthesia is necessary for some other purpose. Spinal anesthesia is similarly useful[9, 10] but must be restricted to good-risk patients who are hospitalized. It is particularly useful in those cases where it is important to study both lower extremities. A satisfactory test is the study of the temperature changes in the area innervated by a peripheral nerve after its effective block with procaine.[11] I frequently employ this test. It should not be used if there is an area of infection or gangrene adjoining the site at which the injection must be made. In many respects, however, the ideal test is the direct blocking of the sympathetic nerves with procaine.[11, 12] It has the advantage over all the other methods in that it permits one to study the effect upon pain of direct interruption of the sympathetic nerves, and I feel that it should always be employed when pain is present. Once complete sympathetic anesthesia is present one can study, in addition to the element of vasospasm and the vascular capacity for dilatation, the effect upon resting pains of all sorts, cutaneous hyperesthesia and tenderness, and intermittent claudication.

In general, one can judge very well by these preliminary studies what operative interruption of the sympathetics to a limb will accomplish. It has been my experience that the principles laid down by Morton and Scott[13] are fundamentally correct: Namely, the nearer the temperature of the previously cooled limb rises to the level to which a normal limb can be brought by the same test, the greater the improvement in circulation that can be obtained from sympathectomy. Where the operative results are not those anticipated from the preoperative studies, the variation is always toward a greater improvement than was anticipated. In recent years there has been a tendency to try the operation in some selected cases which formerly would have been considered unsuitable. Some patients in whom the preoperative sympathetic injection had brought about little or no rise in skin temperature have been sympathectomized with surprisingly good results, although commonly such patients have shown little improvement. One wonders whether in many of these cases

the inconsistency may be due to a poor sympathetic procaine injection. The use of skin resistance studies during the preliminary sympathetic block should help to answer this very important question.

I do not think that skin resistance studies will be necessary as a practical measure in all sympathetic injections. Certainly in studying upper extremities one rarely needs this additional aid, as the efficacy of the block is ordinarily evident from the Horner's syndrome and from the rise in skin temperature in the hand. It will be particularly helpful in lumbar sympathetic injections and especially in those cases in which it appears likely that the circulatory deficiency is largely due to obliterative disease. I think, also, that such studies should be carried out for investigative purposes in a very large number of cases of sympathetic injections. From such a study one might be able to evaluate better the preoperative studies and the postoperative results in regard to improvement in circulation, since one would know with certainty whether the sympathetic injection had given good anesthesia. It would help to elucidate such problems as the delayed response which was discussed in connection with Case 9. It is not at all unlikely that other questions might also be answered.

In addition to the sympathetic injections done in order to evaluate vascular capacity or pain and the aid which might be anticipated from sympathectomy, such injections are helpful in treating certain disorders and are essential in localizing the needles before introducing alcohol where a more permanent chemical sympathetic interruption is desired. Excellent results are being obtained from single or repeated injections of the sympathetic nerves in acute thrombophlebitis,[14] traumatic reflex edema, causalgia,[15] frostbite, and other vascular disorders. Procaine and alcohol injections are very helpful in assuring maximal vasodilatation before operative attack upon certain vascular lesions such as peripheral arterial emboli and aneurysms.[16] Alcohol block of the upper dorsal sympathetics is proving very useful in relieving pain in angina pectoris.[17] In many of these instances it is not essential that the affected extremity be cooled to the point of stabilization of skin temperature before injection, and sometimes such cooling is harmful, but without such exposure of the limb to cold there is always some chance for error in interpreting skin temperature changes as indicative of sympathetic anesthesia. Furthermore, one often desires to carry out such procedures in operating or treatment rooms which cannot be adequately cooled for the usual skin temperature studies. In such cases I believe study of the cutaneous resistance will give prompt and accurate information as to the efficacy of the sympathetic injection. Of course, the warmer the patient is at the time of the injection the more clear-cut will be the difference in cutaneous resistance on the injected and uninjected sides.

SUMMARY

The use of skin resistance studies in determining the accuracy of sympathetic injections is described, and the value of this procedure is discussed.

The author wishes to express to Dr. C. P. Richter, Mrs. B. G. Woodruff, and Miss M. Ascherfeld his appreciation of their cooperation in the skin resistance studies.

REFERENCES

1. Richter, C. P., and Woodruff, B. G.: Changes Produced by Sympathectomy in the Electrical Resistance of the Skin, SURGERY **10**: 957-970, 1941.
2. Levine, M.: Measurement of Electrical Skin Resistance, Arch. Neurol. & Psychiat. **29**: 828-842, 1933.
3. Shumacker, H. B., Jr.: Sympathetic Denervation of the Feet and Legs Occurring Spontaneously or as a Result of Disease, A Preliminary Report, Bull. Johns Hopkins Hosp. In press.
4. Brown, G. E.: The Treatment of Peripheral Vascular Disturbances of the Extremities, J. A. M. A. **87**: 379-383, 1926.
5. Lewis, T., and Pickering, G. W.: Vasodilatation in the Limb in Response to the Warming of the Body With Evidence for Sympathetic Vasodilator Nerves in Man, Heart **16**: 33-51, 1931.
6. Coller, F. A., and Maddock, W. G.: The Differentiation of Spastic From Organic Peripheral Vascular Occlusion by the Skin Temperature Response to High Environmental Temperature, Ann. Surg. **96**: 719-732, 1932.
7. de Takats, G.: The Differentiation of Organic and Spastic Vascular Occlusions, Ann. Surg. **94**: 321-326, 1931.
8. Gibbon, J. H., Jr., and Landis, E. M.: Vasodilatation in the Lower Extremities in Response to Immersing the Forearm in Warm Water, J. Clin. Investigation **11**: 1019-1036, 1932.
9. Morton, J. J., and Scott, W. J. M.: The Measurement of Sympathetic Vasoconstrictor Activity in the Lower Extremities, J. Clin. Investigation **9**: 235-246, 1931.
10. Bull, S., and Lawrence, L. E.: Changes in Temperature of the Lower Extremities Following the Induction of Spinal Anesthesia, Proc. Soc. Exper. Biol. & Med. **27**: 728, 1930.
11. White, J. C.: Diagnostic Blocking of the Sensory and Sympathetic Nerves. A Method of Estimating the Results Which Can Be Obtained by Their Permanent Interruption, Am. J. Surg. **9**: 264-277, 1930.
12. White, J. C.: Diagnostic Blocking of Sympathetic Nerves to Extremities With Procaine, J. A. M. A. **94**: 1381-1388, 1930.
13. Morton, J. J., and Scott, W. J. M.: The Quantitative Determination of Vasoconstrictor Spasm as a Basis for Therapy in Peripheral Arterial Diseases, Ann. Surg. **96**: 754-766, 1932.
14. Ochsner, A., and DeBakey, M.: Thrombophlebitis; Role of Vasospasm in Production of Clinical Manifestations, J. A. M. A. **114**: 117-124, 1940.
15. Homans, J.: Minor Causalgia Following Injuries and Wounds, Ann. Surg. **113**: 932-939, 1941.
16. Gage, M., and Ochsner, A.: The Prevention of Ischemic Gangrene Following Surgical Operations Upon the Major Peripheral Arteries by Chemical Section of the Cervico-Dorsal and Lumbar Sympathetics, Ann. Surg. **112**: 938-957, 1940.
17. White, J. C.: Technique of Paravertebral Alcohol Injection. Methods and Safeguards in Its Use in the Treatment of Angina Pectoris, Surg., Gynec. & Obst. **71**: 334-343, 1940.

ACUTE IODISM DURING THE TREATMENT OF TOXIC GOITER

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IT IS widely accepted by surgeons that iodine for the treatment of toxic goiter is entirely harmless. This belief prevails regardless of the numerous instances, some serious, which occur during treatment in medical clinics.

Barker and Wood[1] first specifically studied 400 cases for unfavorable febrile reaction following oral iodine medication in toxic goiter. In this series there were 7 cases with unquestionable symptoms during the first four to ten days of use. At first appeared redness of the mucous membrane of the throat and nose, with conjunctivitis, temperature elevation, spiking in type, from 100° to 104° F., followed by sweating, itching, and macular rash of most of the body. However, with complete withdrawal of the iodine, symptoms rapidly disappear, except for minor febrile reaction for one to three weeks.

On the other hand, one patient developing iodism on the third day of administration of 3 c.c. of compound solution became markedly worse when the dosage was doubled. There was spread of the rash, desquamation, and hemorrhage into the palate.[2] Later complete withdrawal of iodine, and the institution of vigorous supportive measures failed to alter his course which terminated on the twenty-first day.

Necropsy showed "the skin covered with macular-papular desquamating rash." The thyroid was "enlarged, firm, dry, with many gray-white opacities." The lungs were "congested, with patches of lobular pneumonia. The lymph glands, spleen, liver were enlarged, and microscopically showed miliary inflammatory perivascular lesions" with areas of central necrosis.

Previous to the present illness, five of these seven patients had taken iodine without untoward symptoms, and subsequently, after an interval of months, again tolerated it with benefit.

L. L. D., 40-year-old male, presented himself April 30, 1941, because of nervousness. He had been well until four weeks before, when he had a severe upper respiratory cold, followed by extreme weakness. Shortly after he was jittery and his hands shook, he had profuse sweating, polydipsia, and anorexia. He was irritable, apprehensive, unable to work or concentrate. He lost ten pounds in weight, and for two weeks he had dyspnea, and swelling of the ankles.

At 19 years of age he had a double goiter treated successfully by oral iodine, otherwise he had always seemed well. He enjoyed his work, had good friends, and was happy at home.

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Examination.—Height, 171.7 cm.; weight, 79.6 kg.; temperature, 37° C.; pulse, 106; respirations, 20; blood pressure: systolic 126, diastolic 80. The patient was well developed and nourished. He was cooperative, but excited, and obviously acutely ill. His skin was clear, his eyes markedly prominent with lid lag; pupils reacted normally, and fundi were clear. The mucous membranes of the nose, pharynx, and mouth were clear. There was bilateral, soft, nontender enlargement of the thyroid, which moved upward on swallowing. A bruit was present over the thyroid and there were visible forceful pulsations over both carotid vessels. His heart was rapid, regular, with normal sounds. He had pitting edema of both ankles. Hemoglobin was 13.5 Gm.; leucocyte count, 5,000; urine, negative; Wassermann reaction, negative; nonprotein nitrogen of the blood, 34 mg. per cent; basal metabolic rate +36.

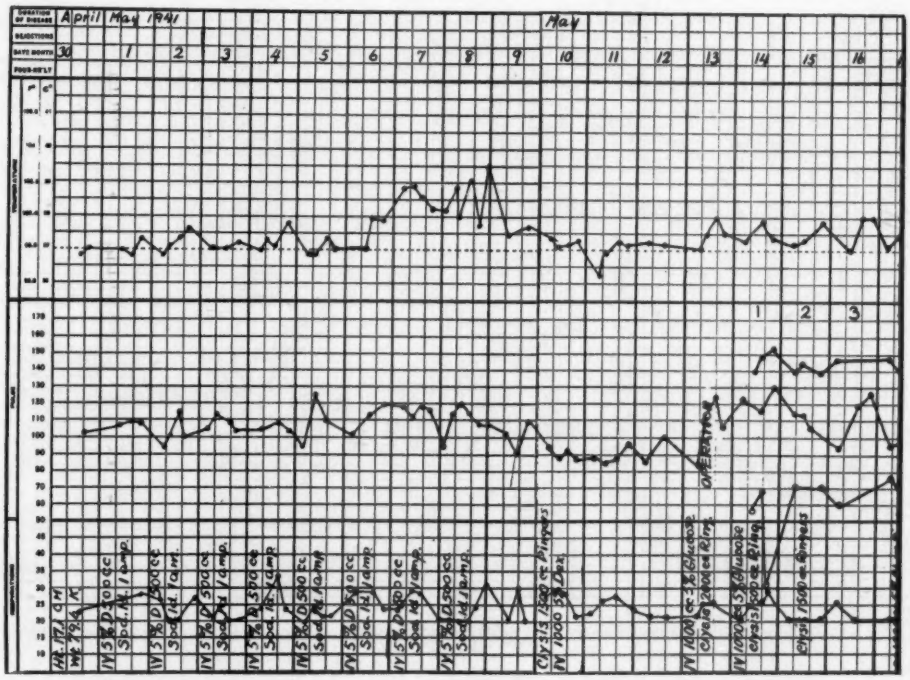

Fig. 1.—Shows febrile response to iodine becoming marked on the sixth day and extending through the eighth day. Immediate return to essentially normal temperature at withdrawal on the ninth day.

The patient was given 1 c.c. Lugol's solution orally three times daily, supplemented by 1 c.c. sodium iodide with 500 c.c. of 5 per cent glucose intravenously. At night he was given 0.1 Gm. phenobarbital. He was on a high caloric diet, and had complete bed rest in a single room.

After five days of comfort, he complained of sore throat with coryza and conjunctivitis the following day. Shortly after there was profuse sweating, increase in restlessness, and apprehension. His temperature increased with each four-hour period to 38.8° C. during the second day of symptoms. Within twenty-four hours however, his condition was alarming, with exacerbation of the symptoms already present augmented by diffuse itching, a macular rash on most of the body, and fever of 39.6° C.

The similarity of the rash to that of chronic iodine poisoning suggested the nature of the disturbance. All iodine solutions were immediately canceled. Rest was ob-

tained by morphine, 0.010 Gm. every four hours, and 2,000 c.c. Ringer's solution was given subcutaneously. Within eight hours of cessation of iodine, the patient was free of itch, fever had fallen from 39.6° to 37.5° C., and pulse dropped from 110 to 90.

Fig. 1 illustrates the rising temperature on the sixth, seventh, and eighth days of hospitalization concurrent with the appearance and exacerbation of symptoms. There was a sharp, crisislike drop at midnight of the eighth day. A basal rate taken on the seventh day was +20.

During the next four days the patient was given daily 1,000 c.c. of 5 per cent glucose intravenously, with 1,000 to 2,000 c.c. Ringer's solution subcutaneously, and sufficient morphine to obtain rest.

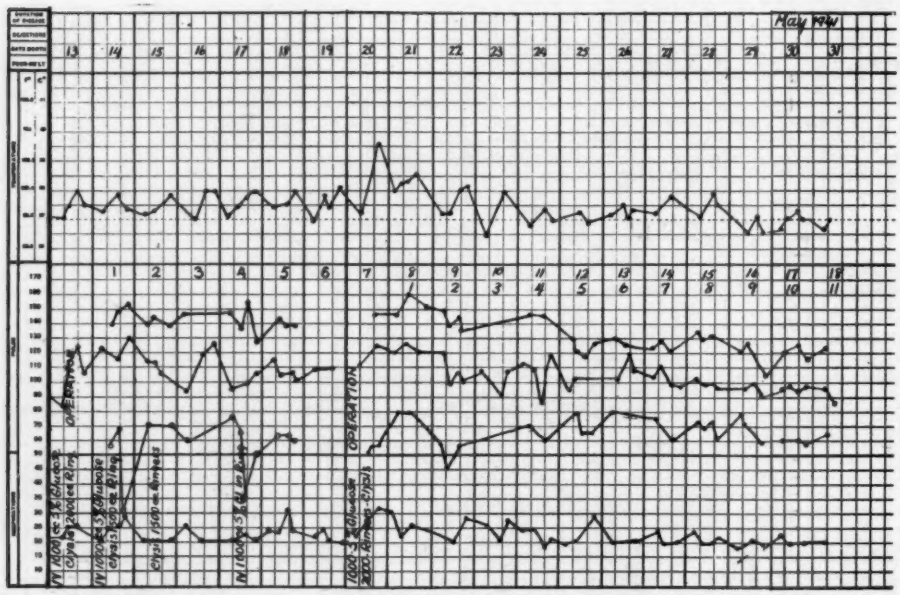

Fig. 2.—Shows postoperative course with a continued minor febrile reaction for two weeks.

On the thirteenth day of hospital care a right hemithyroidectomy was performed without difficulty or reaction, using avertin—gas-oxygen anesthesia. There was, however, a daily afternoon febrile reaction to 38° C. and difficulty in swallowing due to sore throat. The intravenous glucose also was continued, augmented by sufficient Ringer's solution to make the parenteral fluids 3,000 c.c. daily. Seven days later the left lobe was removed with moderate reaction but no evidence of postoperative storm. It had been noted at the second operation that healing was less advanced on the right side than expected. There was considerable serum without fibrin and the skin flaps were edematous. Five days later considerable serum escaped spontaneously from the left angle of the wound. *Streptococcus hemolyticus* and *Staphylococcus aureus* were cultured from this sinus. There was, however, little local inflammatory reaction and no change in his general condition which continued to improve. He was discharged eleven days after the second operation.

Examination of the removed thyroid showed diffuse symmetrical enlargement, each lobe measuring 7 × 5 × 3 cm. The texture was regular and the cut surface homogeneous. The right lobe weighed 50 Gm., the left 40 Gm. Microscopically there

were many small, closely packed acini containing only slight amounts of vacuolated colloid. They were lined by hyperplastic columnar epithelium that was redundant into the lumen. Many groups of small lymphocytes were scattered about.

At home his condition rapidly improved with gain in appetite and weight. After one week, however, he developed quite a marked inflammatory reaction in the left side of the draining wound of the neck, accompanied by pharyngitis. These conditions responded readily to treatment.

The sinus remained even after he was apparently well, and at infrequent intervals extruded spontaneously a silk ligature. At the end of three months, however, he was at his work six days a week, with normal vigor and enthusiasm for this and his private life. A moderate degree of exophthalmos persisted.

There are three types of unfavorable reaction of the individual from contact with iodine. With prolonged use of small amounts a macular-papular dermititis develops which progresses to bulbous and ulcerative lesions if continued. Again certain persons have an intrinsic, marked cutaneous sensitivity resulting in diffuse erythema and swelling if iodine comes in contact with the normal skin. Barker and Wood observed one patient with cutaneous reaction who also had had a febrile manifestation from oral administration, but at a later date was free from both. One patient has been observed whose arm became red and swollen throughout from application of iodine for vein puncture. Lastly, those persons who have what appears to be true allergy to iodine. There is early and violent reaction manifested by mounting fever, irritation of all free mucous surfaces, dermatitis, and nervous irritability. Symptoms disappear rapidly on cessation of iodine, but under forced continuance may become serious or fatal.

In all eight cases reviewed, barbiturate of some form was used concurrent with iodine. However, this would not seem to have a direct bearing for phenobarbital was continued one week following the relief from iodine in this case.

CONCLUSIONS

1. Certain patients with toxic goiter are sensitive to oral iodine.
2. Symptoms of iodism occur early and progress if the drug is continued.
3. The continued use of iodine where there has been a febrile response is dangerous.
4. The basal metabolic rate is affected normally by iodine in persons showing a febrile response.
5. Operation is possible after relief of iodism.
6. Seven cases of iodism in toxic goiter were found in literature and one added.

REFERENCES

1. Barker, W. H., and Wood, W. B., Jr.: J. A. M. A. **114:** 1029, 1940.
2. Moore, G. E.: The Modern Treatment of Syphilis, Springfield, Ill., 1933, Charles C Thomas, Publisher.

FUNCTION OF THE LOWER JAW FOLLOWING PARTIAL RESECTION

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FUNCTION OF THE LOWER JAW

THE lower jaw has multiple functions. These may be divided into support and movement.

The mandible is a hoop-shaped bone anatomically divided into three areas: the ascending rami, the horizontal rami, and the region of the symphysis. It acts as a point of attachment for a number of muscles, most of which are concerned with moving the jaw, but a certain number act from the mandible as a fixed point in moving the tongue.

Movement of the lower jaw is quite complex and takes place in the temporomandibular joints which are combination hinge, ball and socket, and gliding mechanisms. The construction of these joints is such that the lower jaw can open and close, glide forward and backward, and swing from side to side.

As a stationary bone the mandible supports the musculature of the face, maintains a space within which the tongue can function, and with the attached teeth is the structure on which the lips and tongue move in speech and deglutition.

DISTURBANCES IN FUNCTION FOLLOWING PARTIAL LOSS OF THE MANDIBLE

It would seem from the nature of the functions which the mandible performs, that significant losses would seriously disturb function. It has been my experience that this is not necessarily so. Rather large segments of the mandible can be removed without seriously inconveniencing or disfiguring the patient. The loss of function which results depends upon the area of jaw removed and whether or not mouth lining must be sacrificed.

The ascending ramus on one side can be removed with almost no disturbance in function and scarcely noticeable disturbance in facial contour. Such a resection can extend forward to the premolar region of the horizontal ramus without further change in movements of the jaw or sacrifice of its supportive role. In such instances speech is unaffected, chewing is practically normal, and swallowing is undisturbed. There is at times a complaint of soreness in the remaining temporomandibular joint, probably due to strain. The excursion of the jaw is not restricted, but on wide opening there will be a shift of the jaw toward the resected side; this may be no more than the width of an incisor tooth.

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Resection of the horizontal ramus of the jaw likewise causes no serious functional derangement. When the mandible is removed from the angle, or slightly above it, to the midline, there is a moderate inward sag of the soft tissues, which causes some facial asymmetry. This is accentuated by the projection of the cut end of the mandible near the symphysis. It is greater in those instances where the submaxillary gland and lymph nodes must be removed with the bone. Opening of the mouth is not restricted, but there is a shift of the jaw toward the lost side. As it is usually not practicable to wear a denture, mastication is not normal. Nutrition, however, can be satisfactorily maintained even for those engaged in rather heavy manual labor. Swallowing is not affected. Speech is at first blurred due to loss of teeth, loss of sensation, loss of some control of the lower lip on the resected side, and disturbance of the anterior muscular attachments of the tongue. This improves rapidly and in a few months is nearly normal. In these individuals the final speech is usually about that of an edentulous person.

Unlike resection of the ascending and horizontal rami, removal of the anterior, midline projection of the mandible results in marked functional disturbance. If the bone be removed from canine to canine there is a shrinking inward of the remaining halves of the mandible. This destroys the normal occlusion of the teeth, reduces the space in which the tongue can function, and produces noticeable deformity due to loss of support of the soft tissues of the chin. I believe that in order to preserve satisfactory function symphysis, losses of the mandible should be repaired by bone graft. If possible, this should be done at the original operation. However, this is rarely feasible, as in most instances the oral cavity is connected with the wound. In these instances it is best to maintain the horizontal rami on either side in normal relations by interdental fixation and as soon as soft tissue healing permits, insert a bone graft.

If a considerable amount of mucosa is removed with the jaw in any of these areas severe functional disturbance may occur. This is due to the inevitable contractures that develop as the wound heals. In ascending ramus resections with excision of mucosa near the angle, inability to open the mouth is liable to be the end result. After wide excisions of mucous membrane covering the horizontal ramus, the tongue is liable to be drawn forward as contracture occurs, until it protrudes from the mouth. This happens when the excision is forward. If the mucous membrane excision is lateral to the tongue and extends up onto the cheek it may be drawn downward and laterally. Closed bite seriously interferes with nutrition, since a more or less liquid diet is all that is possible. Contractures displacing the tongue affect both speech and swallowing.

INDICATIONS FOR RESECTION

Reference to resection of the lower jaw means the removal of a complete segment so that there is no bony continuity remaining. In a num-

ber of benign conditions affecting the mandible, excision of local areas of the bone is necessary. In these lesions a rim of bone can be left to maintain the arch. If one temporarily immobilizes the jaw, a rim of cortex inferiorly, no more than one-fourth of an inch thick, will suffice. In such cases, the mechanics of jaw opening and closure are not interfered with, although the alveolar ridge is, of course, deformed and special dentures are needed. The common conditions affecting the mandible, in which this local type of bone removal suffices, are dentigerous and dental root cysts, hemorrhagic cysts, giant cell tumor, osteoma, and perhaps small adamantinoma operated upon for the first time.

The indication for extensive resection of the lower jaw is usually the invasion of the bone by the direct extension of carcinoma arising in the

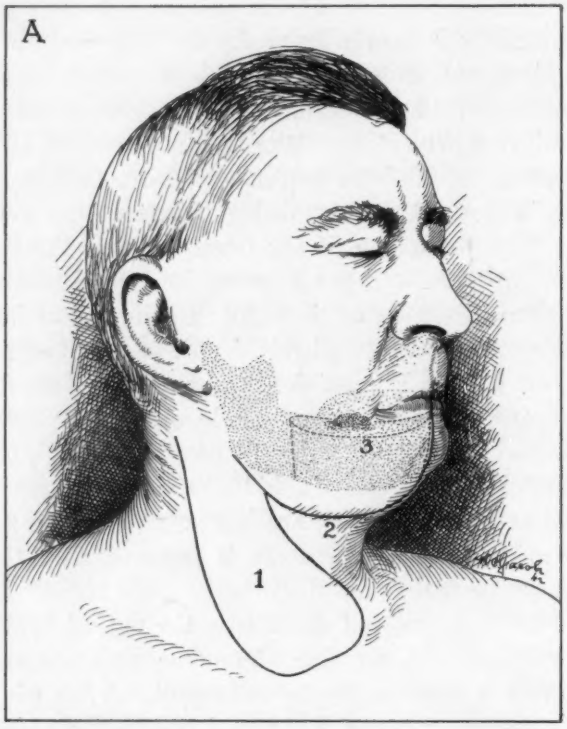

Fig. A.—Diagram of incisions used in excising a cancer of the alveolar ridge invading the mandible. *1*, Flap previously delayed on neck; *2*, incision through midline of lip and extending to angle of jaw. The flap so made is turned externally and allows complete access to the horizontal ramus and the suprahyoid lymph glands. *3*, Area of mandible to be removed.

mucous membrane, or the occurrence of primary malignancy in the bone itself. Infection of the jaw bone is rarely an indication for resection. Osteomyelitis of the mandible is best treated by maintaining the normal arch by whatever mechanical means necessary, draining soft tissue abscesses, and sequestrectomy after sufficient involucrum has formed to maintain the arch. In chronic fibrous nonpurulent osteitis, resection is at times advisable.

OPERATIVE METHODS WHICH PREVENT FUNCTIONAL DISTURBANCE

If possible, the resection should be done intraorally and without sacrifice of mucosa. This can be done in adamantinoma and benign tumors of small size.

In most instances where resection is indicated, it is also necessary to remove soft tissue rather widely. This is best done through external incisions. The majority of these lesions are in the horizontal ramus, and in those instances where a chance of cure seems present and it is

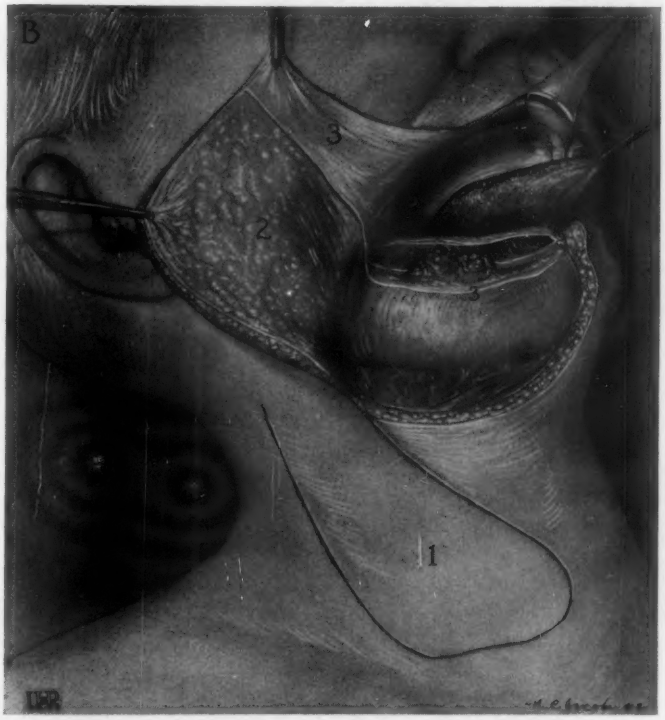

Fig. B.—*1*, Neck flap; *2*, cheek turned laterally; *3*, mucous membrane of the cheek. The growth has been skirted by an incision through the mucous membrane of the cheek and along the lateral border of the tongue.

obvious that a large amount of mouth lining must be sacrificed, plans should be made to restore the lost lining at the time of resection. This is done by developing a flap on the neck prior to excision, or by a free skin graft inserted on a form (Figs. A and D). The approach which I have found most convenient is as follows: The lower lip is split in the midline and this incision carried downward to about the level of the hyoid; from here it turns at a right angle and runs toward the angle of the jaw. The mucosa of the cheek is incised from angle to midline of the lower lip, leaving a wide margin of mucosa and attached soft parts around the growth. Thus a flap of half the lower lip and the cheek is turned laterally allowing complete access to the jaw and mouth. The dissection starts in the neck in order to remove the suprahyoid triangle

of lymph glands en masse with the affected jaw. The jaw is sawed across near the midline and the mucosa incised along the tongue laterally. When the bone has been freed back to the angle, or further if necessary, it is cut across and the growth with the lymph gland area removed in one mass.

If a neck flap has been elevated previously this is now turned upward and used to reline the cheek and area from which the bone has been removed. If a free graft is used this is wrapped around a dental compound model and inserted into the cavity. The flap of cheek and lip is reflected back into position and sutured.

Fig. C.—The involved jaw has been removed with the suprahyoid lymph glands attached. *1*, Neck flap; *2*, cheek turned laterally. The neck flap has been turned upward, rotated, and its edges sutured to the mucous membrane (*3*) of the cheek and to the mucous membrane along the tongue laterally; this neck skin (*4*) now becomes the mouth lining.

CASE 1.—W. E. (S. M. H., No. 126020).

History.—A 63-year-old white farmer was referred to the hospital by his dentist on April 6, 1937, because of a sore on the lower jaw. He stated that in January, 1936, over a year prior to entry, the gum of the right lower jaw became so sore that he had to stop wearing a denture which he had worn for over thirteen years. About a month prior to entry he had consulted his dentist because of increasing pain.

Examination.—The positive findings were limited to the mouth which was edentulous. In about the first molar region of the right lower jaw, there was an eroded, rough, raw area which was surrounded by a slightly raised, firm border. The erosion seemed to extend into the jaw bone. An x-ray of the right mandible (Fig. 1)

showed a moderate erosion of the alveolar ridge. A biopsy was obtained and diagnosed as epidermoid carcinoma.

Treatment.—Because of invasion of the bone, surgical removal was decided upon rather than radiation. In order to resect widely enough to afford a chance of cure, it was thought that it would be necessary to excise a rather wide area of mucosa.

Fig. D.—An alternative method in which a wax form (*1*) with a Thiersch graft wrapped around it is used to replace the excised mucosa. The flap (*2*) is reflected back over this to its original location. The graft resurfaces the raw areas on the flap and joins onto the area of mucous membrane (*3*) which has been left.

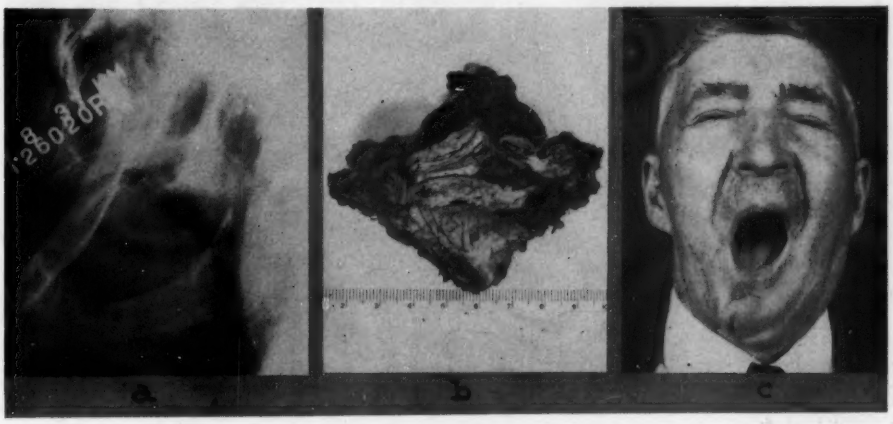

Fig. 1.—Case 1. *a*, X-ray showing erosion of the alveolar ridge, right mandible, due to extension of squamous cell carcinoma of the mucosa; *b*, specimen removed at operation. The ulceration and surrounding mucosa can be seen. The mass includes the horizontal ramus of the jaw, the suprahyoid lymph glands, the submaxillary gland, and adjacent soft tissue. *c*, Functional result four and one-half years after resection. Right cheek lined with skin flap from neck.

The plan was to first elevate a flap on the neck so that tissue would be ready to repair the lining loss at time of resection.

On April 15, a flap was partially elevated and delayed on the right side of the neck. Two weeks later the flap was again elevated under local anesthesia and delayed. In two more weeks the flap appeared to have good circulation and resection and repair were carried out accordingly. This was done in the following manner: The lower lip was split in the midline and the incision continued to the level

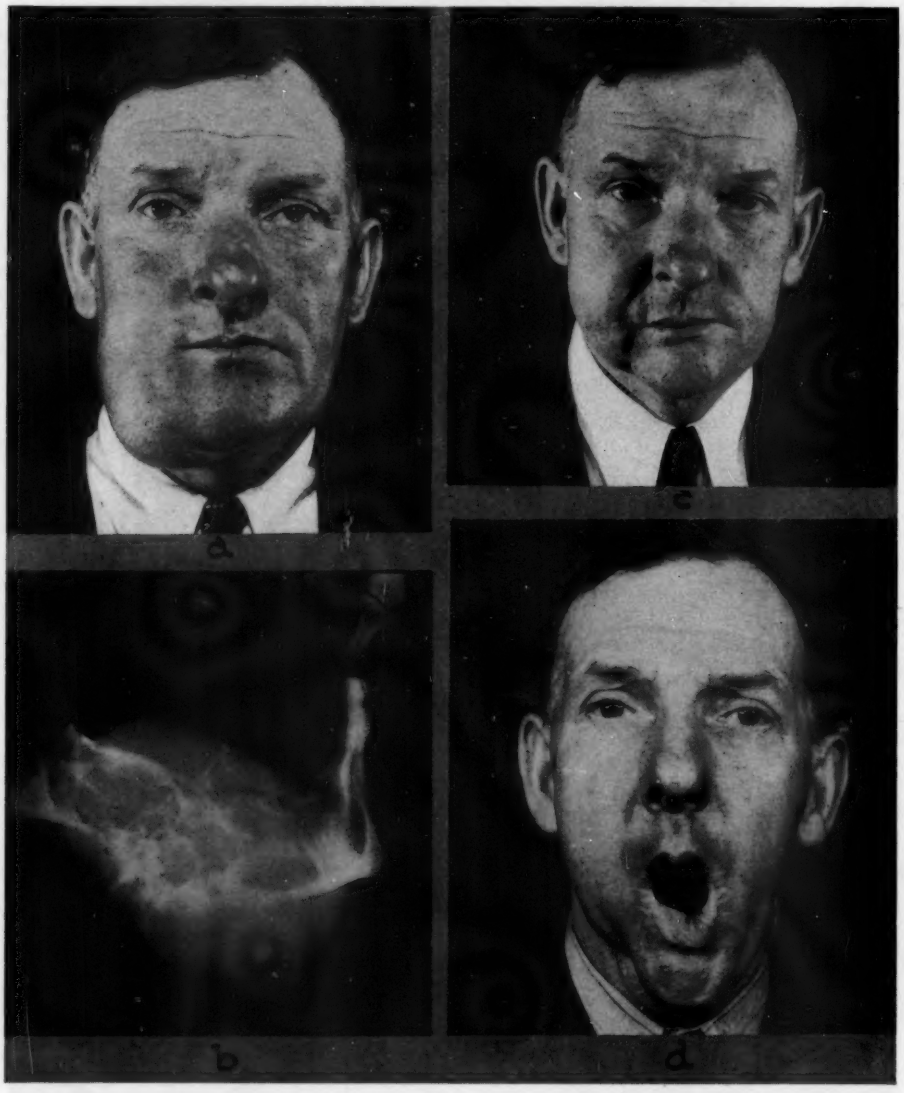

Fig. 2.—Case 2. Resection of large recurrent adamantinoma, right horizontal ramus of mandible, through external incision. Only small amount of mucosa sacrificed which did not warrant replacement. *a*, Size of tumor; *b*, x-ray of excised specimen which shows destruction of mandible and extent of jaw removed; *c*, appearance four years after excision of right side of lower jaw; *d*, function of jaw four years postoperative.

of the thyroid cartilage; it then turned at right angles, to the right, and ended at the right angle of the jaw. Thus, a flap made up of the right side of the face could be reflected, and a large block of tissue containing the mandible from the

third molar to the canine region, the suprahyoid glands, and a wide margin of mucous membrane of the cheek and mouth floor was removed in a block. The flap from the neck was then used to repair the mouth lining (Figs. A, B, and C).

This healed in place satisfactorily except for a minor slough at its tip. Four weeks later the pedicle of the flap was cut and the granulating area on the neck, skin grafted.

Results.—He has been seen at frequent intervals to date, roughly four years after resection. There has been no recurrence. In spite of loss of most of the horizontal mandibular ramus on the right side there is no marked deformity. He speaks intelligibly. He cannot wear a lower denture but has gained weight, which is good evidence that he is able to eat fairly satisfactorily.

CASE 2.—R. M. (S. M. H., No. 57747).

History.—A 49-year-old male, white, engineer, first entered the clinic in February, 1932. About one year before he had noticed a small, hard, nontender nodule on the external surface of the midportion of the right mandible. This gradually grew larger. In December, 1931, it suddenly became greatly swollen, painful and tender, and a large amount of blood-tinged pus discharged spontaneously from about the second molar. He consulted a dentist, who extracted two right lower molar teeth.

Examination.—The positive findings were confined to the mouth and jaw. There were many teeth missing and the remainder were carious snags. There was a hard, round, nodular mass, about 2½ by 1½ inches in size connected with the midportion of the right horizontal ramus of the mandible. X-rays showed a large cystic area in the right horizontal ramus which extended from the second molar region forward to the right lateral incisor. A biopsy was characteristic of adamantinoma. On March 5, 1932, an intraoral local excision of the tumor was done. About one year later a recurrence was locally removed. He was not seen until four years later. He had had during this time a slowly progressive enlargement of the right jaw. I saw him for the first time in June, 1937. He then had a very large tumor involving almost the entire horizontal ramus of the right lower jaw. X-rays (Fig. 2*b*) showed cystic areas from the angle of the jaw almost to the symphysis. I advised resection.

Treatment.—The tumor was exposed through an external incision after placing a tape around the external carotid. The entire mass was removed from a little to the left of the symphysis to well past the angle, about one inch of the ascending ramus being removed. The mucous membrane in the mouth was left intact except for a small longitudinal strip over the midportion of the tumor, and could be closed by suture.

Results.—This man's case has been followed closely. He was last seen on May 8, 1941, and has had no recurrence. There is moderate sinking in of the right side of the face. The jaw shifts slightly to the right on wide opening (Fig. 2*d*). He does not wear a lower denture, but is able to do hard physical labor and has maintained his weight satisfactorily. Speech is normal except for the lisp associated with toothlessness.

CASE 3.—V. W. (S. M. H., No. 107153).

History.—I first saw this 12-year-old schoolgirl in September, 1935. About nine months prior to this she began to have a painful swelling of the left lower jaw. This had gradually become so constantly painful that she was continually taking salicylates for relief. She was unable to chew because of pain and had lost about eight pounds during the three months prior to entry. This swelling seemed to be intermittent in character.

Examination.—There was no fever or any other constitutional signs of infection. There was a diffuse, firm enlargement of the left horizontal ramus from above the angle to about the first bicuspid. This was tender. The soft tissues over the bone did not appear thickened (Fig. 3*a*). The teeth were in excellent condition. The lymph glands in the left upper neck were enlarged, firm, and tender. There was no leucocytosis, and the Wassermann was negative. X-ray of the lower jaw showed diffuse increase in width and thickness, with spotty areas of decreased density (Fig. 3*c*). It was suspected that the disease was a low grade infection of some nature

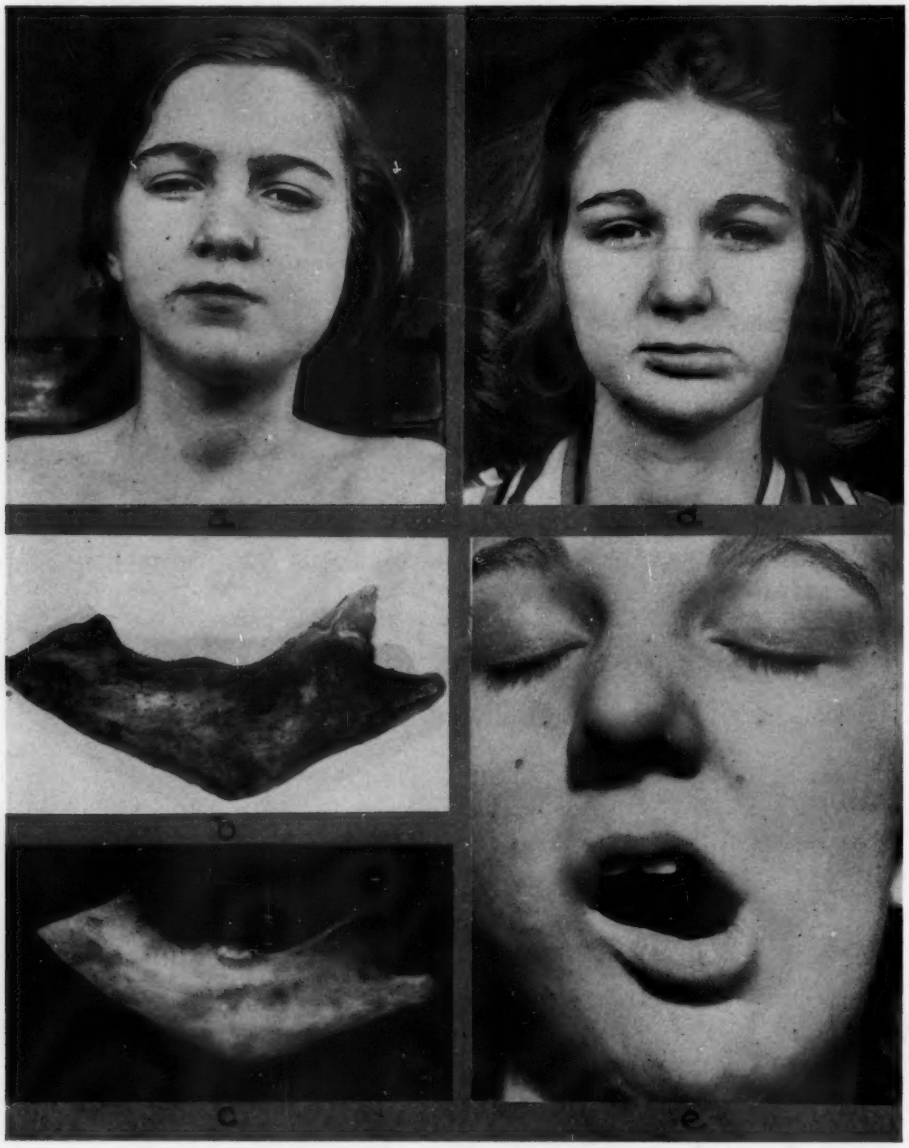

Fig. 3.—Case 3. *a*, Enlargement of left side of face due to chronic fibrous osteomyelitis of mandible; *b* and *c*, specimen and x-ray of specimen removed. This left side of the jaw from the condyle to a little past the mental foramen is diffusely expanded. The x-ray shows multiple areas of decreased density. *d*, Appearance two years after operation. The jaw was removed subperiosteally and there has been a partial regrowth of the bone. *e*, There is a moderate shift to the shortened side on opening.

but a definite diagnosis could not be made. During December, 1935, the body of the mandible was explored through an external incision. The periosteum was thickened, the bone was greatly enlarged and its surface roughened. In several areas there were cortical perforations. By enlarging these it was found that the bone was spongy and soft. No pus was found. A culture was taken which proved negative and bone which was removed was diagnosed as chronic fibrous osteomyelitis.

The child was then seen at frequent intervals during 1936. In October of that year it became evident that she was progressively getting worse. The jaw had slowly enlarged, opening of the mouth becoming limited, and she was in almost constant pain. She was taking salicylates in large doses. X-rays showed progressive increase in the spotty areas in the bone and an increase in size. It was decided to resect the involved bone.

Treatment.—In November, 1936, the bicuspid and molar teeth were extracted and the sockets healed without trouble. About six weeks later, after the sockets were thoroughly healed, resection was done through an external incision. The left temporomandibular joint was disarticulated and the bone cut across just medial to the mental foramen (Fig. 3*b*). This resection was accomplished subperiosteally without entering the mouth. The right side of the jaw which remained was held in correct occlusion by interdental wiring. She gradually regenerated a small horizontal ramus and an ascending ramus up to about the coronoid notch. About a year after resection she began to complain of pain in the chin region and this area became swollen. X-rays showed an extension of the same process into the right side of the mandible as far as the right first molar. It was thought that removal of this involved bone would be necessary, and the remaining teeth on the right side were extracted. Following this there seemed to be some decrease in pain and swelling, and resection of the right side was deferred.

Results.—She was seen frequently for about two years after the extractions. She had recurrence of swelling and pain but there was a gradual improvement in symptoms. In December, 1940, x-rays showed a complete disappearance of the mottled areas in the right mandible. The left mandible had regenerated except for the condyle and coronoid process. There was a moderate sunken appearance of the left side of the face and pronounced shift of the jaw to the left on complete opening (Fig. 3 *d* and *e*). It was decided that a lower denture should be made. This is in process.

CASE 4.—W. W. (S. M. H., No. 125015).

History.—This 42-year-old white hotel clerk entered the clinic in February, 1937. He complained of pain in the left lower jaw. He began having trouble with the jaw about eight years before. At that time he had an impacted wisdom tooth and a small cyst removed from the lower jaw on the left. About four years later a growth developed in the same region and was removed. He then had no difficulty until about one week prior to my first seeing him. At this time he complained of pain and a sensation of the jaw being broken.

Examination.—At that time there was no visible or palpable swelling, but an x-ray of the left ascending ramus of the mandible showed a large cystic area replacing the ascending ramus (Fig. 4*a*). Other than an old poliomyelitic atrophy of the left lower leg, the remainder of the examination was negative.

Treatment.—The angle and ascending ramus of the left mandible were exposed through an external incision. There was a large cyst in the ascending ramus. There was no bone on the medial side of this tumor and only a thin eggshell-like bony wall externally. This cavity contained only a small amount of tumor tissue, but a large amount of brownish, moderately viscous fluid. The condyle did not seem to be greatly involved, but had no bony connection with the remaining jaw, conse-

Fig. 4.—Case 4. Recurrent adamantinoma of ascending ramus, left jaw. Excised through external approach without entering mouth. *a*, X-ray showing large cystic area in ascending ramus; *b*, postoperative x-ray showing absence of ascending ramus; *c*, appearance four years after excision and shortly after removal of soft tissue recurrence; *d*, almost no disturbance in function. The only abnormality is a slight shift of the jaw toward left on wide opening.

quently, it and the coronoid process were completely removed. All suspicious bone fragments and soft tissue were removed, leaving a jaw which had no bone from the angle of the horizontal ramus upward (Fig. 4*b*). The tumor tissue removed was characteristic adamantinoma.

Results.—He recovered promptly and without difficulty. He was seen for a few months after operation and had no particular complaints. About four years later, in March, 1941, he reappeared with a large swelling in the parotid region on the left. This had come to his attention for the first time about two months before. He had no particular pain and the jaw function had not been disturbed. He was again operated upon and a large cyst with small intramural tumors was removed; this, too, was adamantinoma. This operation was rather difficult and the patient had a stormy immediate postoperative course, due to shock from blood loss. He recovered and is at present back at his former job as a hotel clerk. He has good function of the jaw and has had for the past four years, without an ascending ramus. He can chew anything, has no pain, and the only abnormality on examination is a light shift of the jaw to the left on wide opening (Fig. 4*d*).

CASE 5.—C. K. (S. M. H., No. 154820).

History.—This 79-year-old retired Irishman complained of pain about the angle of the left lower jaw and a small ulceration of the gum in this region. About a year before he first came to me in September, 1939, he had begun to have intermittent soreness of the gums and would occasionally omit wearing his lower denture for about a day or so. About six months later he noticed a tiny ulceration in the left lower gum posteriorly. This had never bled, and had increased only slightly in size. For the past two months he had not worn his lower denture because of discomfort.

Examination.—He was a well-preserved, mentally alert old man. The mouth was edentulous. There was a small ulceration about 1 cm. in diameter on the left lower alveolar ridge in about the location of the third molar. There was a firm, hard enlargement of the angle of the mandible which seemed to extend upward in the ascending ramus. X-rays showed an area of bone destruction, multilocular in character, near the angle of the left jaw; this seemed to extend upward toward the condyle. A small piece of tissue was secured from deep in the ulcer for microscopic examination. There was considerable discussion about the diagnosis of this biopsy, but most of the pathologists thought it was a carcinoma of the cylindroma type.

I thought that the x-ray and the clinical course indicated an adamantinoma and I advised local excision on that basis.

Treatment.—At operation an incision was made intraorally around the ulcer, and a cystic area in the mandible at the left angle was exposed. It was found that this contained a firm cellular tumor not characteristic of adamantinoma. A frozen section was made and it was evident that the tumor was a carcinoma of glandular type. It was also found that this tumor extended upward as far as one could reach into the ascending ramus. It was therefore decided to resect the involved portion of the jaw. The joint on the left was disarticulated, the body of the mandible cut across in the bicuspid region and this portion removed (Fig. 5*a*). This was completed through the original intraoral approach. Sections of the specimen were examined and diagnosed as carcinoma of the cylindroma type replacing bone marrow.

Results.—He recovered promptly and was able to be on a soft diet on the twelfth postoperative day. Since then he had been seen frequently. He complains of numbness of the left lower lip and a feeling of tightness on the left side on opening. He at times complains of some soreness in the right temporomandibular joint. There

is no noticeable deformity (Fig. 5*b*). There is a slight shift of the jaw to the left on opening. He has been able to maintain his weight satisfactorily and as yet, one and one-half years later, there is no evident recurrence. He does not wear a lower denture.

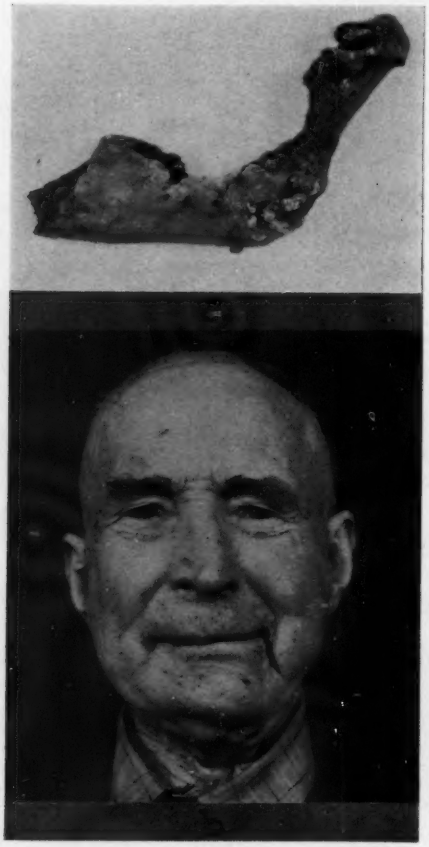

Fig. 5.—Case 5. Intraoral resection of the left mandible from condyle to bicuspid region for cylindroma. *a*, Specimen removed. The mandible has been partially destroyed by the growth. *b*, Appearance two years after resection. Unfortunately a photograph showing function was not obtained, but the patient does have satisfactory opening with only moderate shift to the left.

Case 6.—I. K. (S. M. H., No. 153369).

History.—This 34-year-old housewife was sent to us for an opinion and treatment in May, 1939. About one and one-half years before she had noticed a slight swelling of the right side of her chin, and soreness of the lower incisor teeth. She consulted a dentist who x-rayed the jaw and told her that she had a tumor of the bone. In December, 1937, a surgeon removed the tumor. Following this there were four recurrences and excisions at about sixty-day intervals. Following the fifth excision the growth again grew rather rapidly. Pathologic examination of the previously removed tissue was reported to us as osteogenic sarcoma.

Examination.—When we saw her some one and one-half years after onset, and with her sixth recurrence, there was an obvious firm mass involving the anterior projection of the mandible. It involved most of the body on the right, and extended into the horizontal ramus on the left to about the canine region. In the central portion of the tumor there was infiltration of the skin, but no ulceration.

An x-ray of the jaw showed the typical shooting-star radiations of bone characteristic of osteogenic sarcoma (Fig. 6*a*).

Treatment.—Because of the repeated recurrences, the nature of the growth, and the proximity to skin it was decided to resect the bone and soft tissue of the chin in one block, recognizing that repair of soft tissues and bone would be necessary. In May, 1939, this was done preserving only the hypoglossal nerves and the vermilion border of the lower lip. Following this the soft tissues were reconstructed in four steps (Fig. 6*c*). Following the last operation, at which flaps from the neck had been turned up in place to form mouth lining and skin of the lower face, the patient about two hours after operation suddenly became apneic and died. It was thought that death was due to obstruction of the airway. Post-mortem examination showed no demonstrable metastases.

Fig. 6.—Case 6. Resection of mandible from angle to angle with involved soft tissues because of osteogenic sarcoma. *a*, Typical x-ray appearance of osteogenic sarcoma of mandible; *b*, excised specimen. The major portion of the growth involves the symphysis. *c*, Appearance of patient two weeks after resection. In this type of resection repair is, of course, imperative. In this instance, lining and covering of the cheeks and skin were reconstructed from three separate neck flaps, and following this a bone graft had been contemplated. The patient died of respiratory difficulty a few hours after the fourth step. A post-mortem showed no demonstrable metastases. In this type of resection, replacement of bone is necessary for both function and appearance.

CASE 7.—R. B. (S. M. H., No. 157559).

History.—This housewife, 65 years of age, began to have pain in her right jaw and ear about fifteen months before I first saw her in September, 1939. She went to three different dentists and had her lower denture altered, but without relief. Her family doctor, whom she then consulted, advised her to have an x-ray of the jaw. This showed an impacted wisdom tooth which was extracted in January, 1939. The tooth socket healed slowly, and about March, 1939, a swelling of the jaw developed. An x-ray was again taken and she was told that she had a tumor of the jaw. She was then given deep x-ray therapy to the right lower jaw for a number of months. Her pain, however, persisted. The swelling she believes may have increased slightly. She then consulted me.

Examination.—She was a very thin woman who appeared older than 65. The right side of the jaw was noticeably swollen (Fig. 7*a*), this swelling extending down into the submaxillary and submental region. The mouth was edentulous. A little to the midline there was a puckered, burrowing ulcer about 2 cm. in diameter on the alveolar ridge. The base of this ulcer was friable and bled easily. An x-ray of the jaw showed that the bone in the bicuspid region was almost completely severed by the ulceration (Fig. 7*b*). A biopsy of the ulcer base showed squamous cell carcinoma.

Treatment.—This lesion should have been considered inoperable because of the wide extension into soft parts, but in an attempt to relieve her of pain, resection was done in October, 1939. It was obvious that a large amount of the mouth lining would have to be removed, but because of the small chance of cure it was decided to disregard repair of this. The resection was done in block fashion, from a little anterior to the angle of the jaw on the right to slightly past the midline on the left. The submaxillary and submental lymph glands were removed with the section of jaw, as well as the mouth floor on the right and anteriorly (Fig. 7*c*). The

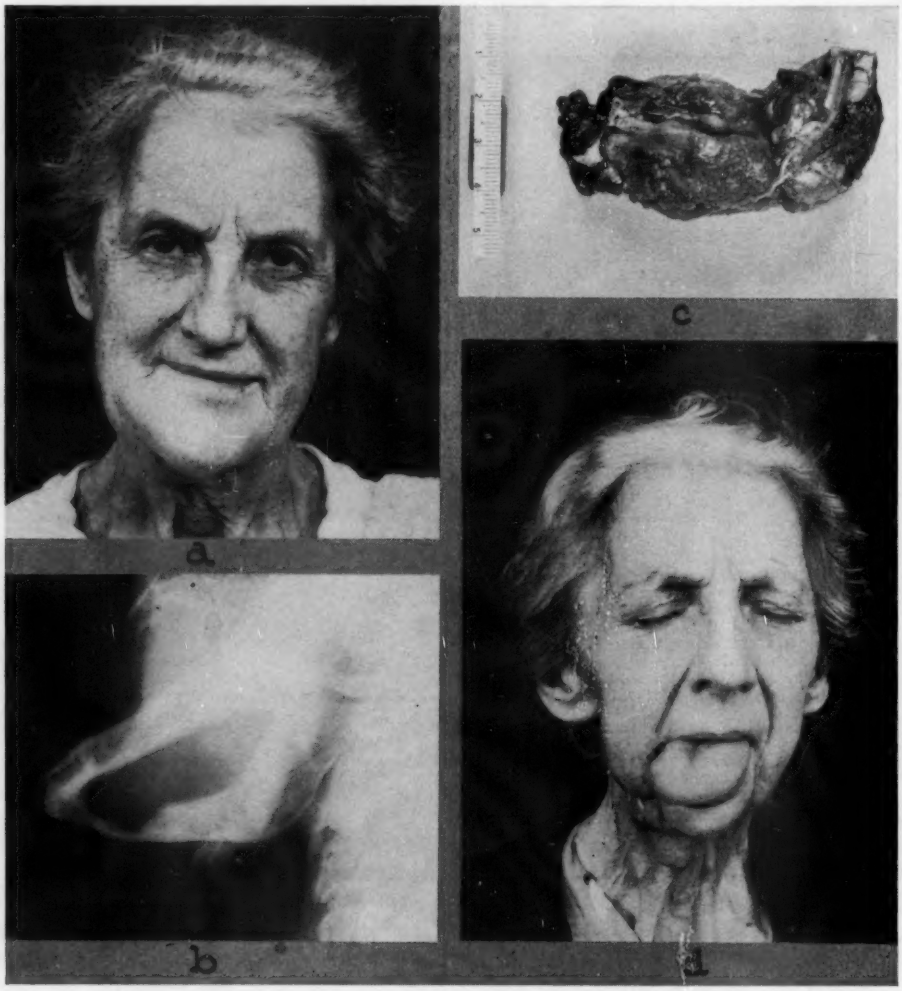

Fig. 7.—Case 7. Advanced carcinoma of right alveolar ridge. *a*, The growth has extended into soft tissues causing a noticeable enlargement of the right side of the face; *b*, the x-ray confirms the extent of the growth. It has eroded through almost the full width of the bone. *c*, The specimen includes the horizontal ramus and lymph gland area; *d*, protrusion of the tongue and difficulty in swallowing were the main complaints postoperatively. This was due, I believe, to a wide removal of mucosa without replacement, and not to recurrence which was present one and one-half years after resection when this photograph was obtained.

growth was found to invade the undersurface of the tongue, and the right hypoglossal nerve had to be sacrificed along with a portion of the undersurface of the tongue. This left a large area on the right and under the tongue denuded of mucous membrane. This was closed under considerable tension, and in so doing

the tongue was drawn quite far forward. The immediate course was quite stormy, characterized by difficulty in breathing as well as in the ingestion of food.

Results.—She recovered slowly and for about a year was free of pain. However, she had been quite uncomfortable during this entire period due to a gradual protrusion of the tongue, which was accompanied by what appeared to be a lymphedema of the right half of the tongue. About fifteen months after operation she again began to complain of pain, and there was an obvious recurrence in the soft tissues of the neck on the right side. She was given deep x-ray therapy with moderate relief. She is still living about one and one-half years after operation, but in pain. At no time has function of her jaw been satisfactory. This, I attribute, not to the bone loss, but to failure to provide for the large loss of lining. This allowed the tongue to become adherent in a contracted, forward position, which interferes greatly with swallowing and speech.

CASE 8.—F. H. (S. M. H., No. 173353).

History.—A 60-year-old white, male, bartender was referred to me on June 21, 1941, because of a recurrent squamous cell carcinoma in the floor of the mouth on the right side.

Fig. 8.—Case 8. Carcinoma of right alveolar ridge rapidly recurrent following x-ray therapy and local surgery. *a*, Appearance after resection of right horizontal ramus and replacement of mucosa by a free skin graft on a stent; *b*, function is not greatly impaired.

Fourteen months before, he had a lower right molar tooth extracted because of pain. Six weeks later another molar tooth was extracted from the same region. About one month later he noticed a growth along the alveolar margin where the teeth had been extracted. This gradually increased in size but caused him no pain and there was no bleeding. He consulted numerous physicians and dentists during this period, but evidently the diagnosis was not suspected. In January, 1941, a positive diagnosis was made of squamous cell carcinoma by biopsy. In addition, a

four plus Wassermann reaction was obtained. The lesion in the mouth was treated between Jan. 8 and Feb. 5, 1941, with 6000 r. x-ray with an intraoral cone in divided doses of 300 r. The usual local reaction followed this therapy with disappearance of the tumor.

On March 19, six weeks after completion of the course of x-ray therapy, there was an obvious recurrence along the alveolar ridge. An x-ray of the right mandible at this time showed no invasion of the bone. On April 3, 1941, a right suprahyoid neck dissection was done and the intraoral recurrence removed locally. Microscopic examination of this tissue showed typical squamous cell carcinoma of oral mucosa and questionable lymph gland involvement.

On May 20, 1941, about six weeks after the local excision, a recurrence was evident. He was referred to me at that time.

Examination.—The general examination was negative except for a four plus Wassermann. Local examination showed the neck incision well healed. There was a definite swelling of the soft tissues over the midportion of the right horizontal ramus. There was friable, vascular tumor about the neck of the first bicuspid tooth. The alveolar ridge was bare and necrotic from this tooth to the angle of the jaw, and in the adjacent mucous membrane in the region of the first molar there was a patch of tumor. It was evident that there was a recurrence of the growth extending into the soft tissues lateral to the jaw. A radical excision was advised.

Treatment.—On June 31, 1941, a block resection of the involved area was done. After extracting the left lateral and central lower incisors, the lip was split in the midline to the hyoid. A connecting incision from the angle of the jaw to the lower end of the vertical incision was made. This flap of tissue was reflected laterally leaving a wide margin of normal mucous membrane around the horizontal ramus (Figs. A and B). The jaw was cut across through the area of extraction, and through the ascending ramus about one inch above the angle of the jaw.

An incision was made in the mucous membrane along the tongue laterally and around the angle of the jaw to join the lateral incision. The mass of soft tissue and bone was lifted out in one piece. The flap was sutured back in place and the raw interior covered with a large, split, thick skin graft on a wax mold (Fig. D).

Results.—He had a rather difficult postoperative course. Due to difficulty in swallowing he lost about thirty pounds of excess weight. The graft took fairly well and he gradually gained strength and freedom of tongue action. In two months he returned to his old job as a bartender and is still performing his duties satisfactorily. He has now gone about eight months without recurrence.

He has free opening of the mouth, but is unable to wear either an upper or lower denture. In spite of this, his nutrition is good and he is able to work. The right side of the face is noticeably sunken and a prosthesis to hold the cheek out in normal position is to be constructed.

SUMMARY AND RESULTS

The mandible has functions of support and movement. These are intimately related to appearance, speech, chewing, and swallowing. The ascending or horizontal ramus of the lower jaw, or both, can be removed without too seriously impairing function. If the symphysis region is excised, great disturbance in function results unless the bone loss is repaired.

If a considerable amount of soft tissue and mucosa is removed with the resected bone, functional disability ensues. This can be prevented by repair of the mucosal loss without bone replacement.

Editorial

Traumatic Injuries to the Peripheral Vessels in Both Civil and Military Practice

THE incidence of injuries to the peripheral vascular tree will be greatly increased because of the large number of nations at war today. In peace time these injuries are usually treated by physicians trained in vascular surgery, whereas in time of war they are cared for largely by the general surgeon. For these reasons, it is absolutely necessary that all medical officers in the armed forces be thoroughly cognizant of the pathologico-physiologic conditions induced by arterial and arteriovenous injuries, as well as of the principles underlying the successful management of these cases. Proper treatment will reduce the loss of life and limb to a minimum, thus enabling a larger number of men to return to active or limited duty.

In modern warfare, high explosive and bullet injuries to the vascular tree in the extremities are liable to be excessive. These injuries range from simple contusion with segmental spasm to complete severance and destruction of the main peripheral vessels. Contusion of vessels is preceded by soft tissue bruises made by shell fragments or bullets passing through the tissues without primarily involving the vessels. The explosive force is transmitted to the vessel wall by continuity of tissue. This results in intramural bleeding with secondary luminal thrombosis or degenerative changes in the vessel wall which gradually give way to produce an aneurysm. In a number of cases there is not only intramural bleeding but rupture of the intima with rapid vascular occlusion by thrombosis. Therefore, a wide range of vascular lesions are produced by contusions, differing only in degree and extent, with a similar range in the incidence of permanent changes, that is, from segmental spasm or partial and complete thrombotic luminal occlusion to late aneurysmal formation.

Direct injuries result in partial or complete severance of the vessel wall, with or without complete segmental loss of the arterial wall and accompanying veins. The immediate effect of this type of injury depends upon whether the wound is semiclosed (puncture wound, bullet or fine shell fragment) or is widely lacerated or open. In the former, there is immediate bleeding into the perivascular tissue with hematoma formation. Bleeding is stopped by pressure of the hematoma upon the

vessel as well as segmental vasomotor spasm which contracts the vessel at the site of injury. After days or weeks the hematoma forms a pseudoarterial aneurysm. Therefore, every localized hematoma associated with a punctured wound should be considered a potential arterial aneurysm. Occasionally, this type of arterial injury continues to bleed into the tissue and muscular planes to produce irreversible shock resulting in death of the patient. I have seen three such cases.

In lacerated wounds with considerable segmental destruction or severance of the vessels, the patient may succumb from hemorrhage and shock (which is usually the case during battle), or shock may occur, lowering the blood pressure to such a degree that bleeding automatically stops. This may save the patient's life if local and systemic treatment can be instituted before shock becomes irreversible.

When the vein as well as the artery is injured, the peripheral and central blood streams are converted into a common pool. A hematoma forms and a firm tumor mass results. After days or weeks an arteriovenous aneurysm appears. This type of aneurysm has both local and systemic effects and differs from the pure traumatic arterial aneurysm in that the latter has no cardiac effects. The cardiac condition resulting from an arteriovenous aneurysm is at times sufficient to produce cardiac decompensation. This depends entirely upon the size of the vessels, the size of the arteriovenous opening, and the proximity to the heart. Therefore, in all traumatic injuries to the peripheral vessels, the occurrence of both pure arterial and arteriovenous aneurysms should be anticipated.

The peripheral vascular tree is controlled by the sympathetic nervous system which contains both vasomotor constrictor and dilator fibers. Stimulation of the system at any level along its peripheral course produces spasm of the vessels supplied, whereas destruction or blocking of the constrictor fibers results in vasodilatation of the vessels. This applies to both arteries and veins. Therefore, an injury to the peripheral vessels will result in segmental spasm. This may be sufficient to produce luminal obliteration which may persist long enough to produce thrombotic occlusion of the artery and all of its pathologic consequences. The point of injury of the vessel frequently acts as focus for initiating a spreading vasomotor spasm which involves not only the main peripheral arteries and veins but all of their branches as well. If spasm of the vessels continues for a long time, obliteration of the vasa vasorum occurs to prevent vessel wall nutrition and invoke internal changes resulting in thrombosis, ischemic gangrene, and loss of limb.

In order that proper treatment may be instituted, a thorough understanding of this pathologic physiology is not only essential but absolutely necessary. Five fundamental principles should be observed in the management of traumatic injuries of the peripheral vascular tree: absolute control of hemorrhage, treatment of shock, surgical correction of the injury, treatment of arterial and arteriovenous aneurysms,

and control of the sympathetic nerve supply to the peripheral vessels.

Hemorrhage can usually be controlled by a tourniquet or by local compression bandages. This will suffice until aseptic surgical procedures can be undertaken. Shock should be combatted by plasma infusions and blood transfusions. Plasma infusions can be given at any time or place because of the modern methods of processing, storing, and transporting plasma. Thus, plasma infusions are preferable to blood transfusions, because the use of plasma obviates the necessity of delay.

Surgical treatment of the injury should be performed under aseptic conditions. In puncture wounds with vascular injury, it is advisable to operate in the first few hours even if hemorrhage has not been controlled. If this is not possible, operation should be deferred until the hematoma has organized. The resulting arterial or arteriovenous aneurysm can be treated at a later date. From three to six months later is the optimal time.

Lacerated wounds with or without destruction of the vessels should be debrided, sulfanilamide sprinkled into the wound, and the vessels ligated. Arterial suture is a highly developed art which consumes time, and, as a rule, thrombosis occurs at the suture line. Therefore, in war, arterial continuity restored by suture is seldom indicated.

The late sequelae of arterial and arteriovenous traumatic injuries are arterial and arteriovenous aneurysms. These pathologic clinical entities should be treated according to the methods of Matas. The exception to this "postponement rule" is an acute arteriovenous aneurysm in which there is an extensive opening between the large caliber vessels, and in which cardiac dilatation is rapidly taking place. Here, simple ligation of the proximal vein will tide the patient over this distressing complication and the arteriovenous fistula can be repaired at a later date.

The fifth and, I believe, the most important factor is control of the pathologic function of the sympathetic nerve supply to the peripheral vessels. Maintenance of collateral circulation, segmental as well as diffuse vasomotor spasm of the peripheral arteries and their branches is controlled by preventing vasospastic impulses from reaching the main arteries and veins. This fundamental principle, if observed, restores adequate blood volume flow through the main arterial stem and its branches and thereby prevents ischemic gangrene.

When a patient has an injury in the peripheral vascular tree, the peripheral pulse should be thoroughly investigated. If it is absent, vasomotor spasm is present and is of major importance. Regardless of the type of vascular wound, blocking out the sympathetic ganglionated chain by chemical means (1 per cent novocain, or novocain and alcohol, 95 per cent) is urgently indicated. Sympathetic block should be repeated once or twice in the twenty-four hours and continued until arteriovenous spasm has been overcome and the tissues distal to the injury are adequately nourished. For the lower extremity, the first to

the fourth lumbar sympathetic ganglia should be blocked, and for the upper extremity the stellate ganglion should be injected. We have used this method in all traumatic injuries of the peripheral vessels as well as for aneurysms for the past twelve years without the occurrence of a single case of ischemic gangrene.

In recapitulation, in all traumatic injuries of the peripheral vessels, hemorrhage should be stopped by a tourniquet or compression bandages, shock prevented or overcome by plasma infusions and blood transfusions, injured vessels repaired or ligated, vasomotor spasm of the vessels prevented by sympathetic block, and arterial and arteriovenous aneurysms treated by the accepted methods of Matas.

—*Mims Gage, M.D.*
New Orleans, La.

Review of Recent Meetings

THE SOCIETY OF UNIVERSITY SURGEONS

THE Fourth Annual Meeting of the Society of University Surgeons was held at the Cincinnati General Hospital and Children's Hospital, Feb. 12-14, 1942.

On the first day, Feb. 12, 1942, there was a general inspection of the Department of Surgery of the University of Cincinnati and presentation of interesting cases and problems under investigation by the local group.

During the sessions held on February 13 and 14 papers were presented by various members and these appear in this number of the journal. Papers presented and not published, or read by title include:

Franklin E. Walton (Washington University): Auxins in Relation to Certain Phases of Wound Healing.

Edward S. Stafford, and John Staige Davis (Johns Hopkins): Successful Construction of a Complete Extrathoracic Esophagus.

William F. Rienhoff (Johns Hopkins): A Clinical and Experimental Study on the Closure of the Primary Bronchus Following Total Pneumonectomy.

Alexander Brunschwig (Chicago): The Operative Treatment of Cystadenomas of the Pancreas.

Book Reviews

Accidental Injuries. By Henry H. Kessler, M.D., Ph.D., F.A.C.S., Ed. 2. Pp. 803, with 202 illustrations. Philadelphia, 1941, Lea and Febiger Co. $10.

This is a book of 803 pages with 202 illustrations and is concerned mainly with the physician's responsibility in the interpretation of the medicolegal aspects of workmen's compensation and public liability. The author has first presented a discussion of laws and rules followed by a surgical and medicolegal discussion of injuries in every part of the body. He has also discussed diseases and poisonings which may arise among workmen and be attributed to occupations. Numerous court decisions are presented in illustration of various injuries.

It is impossible to review in detail or even list the numerous subjects covered. This book is a very useful reference for the inexperienced or experienced practitioners who may be called to report upon or testify in workmen's compensation injuries and diseases and in public liability cases.

Neuroanatomy. By Fred A. Mettler, A.M., M.D., Ph.D., Professor of Anatomy, University of Georgia School of Medicine. Pp. 476 with 337 illustrations. St. Louis, 1941, The C. V. Mosby Co. $7.50.

This text is written for the medical student with a view to preparing him for clinical medicine. Consequently, it provides a useful reference book for the physiologist, neurologist, and neurosurgeon. The first portion of the book deals with the topography and morphology of the central nervous system as seen with the naked eye. Throughout this section attention is continually drawn to those general anatomic relationships and concepts which form the basis for the manipulations of practical medicine.

The second part of the work, which is the microscopic section, concerns itself with the establishment of a sound and usable functional viewpoint. Special attention has been given to the matter of terminology. No new terms are employed at any place in the text without having been previously defined.

A carefully chosen list of references is included, with definite preference shown to articles in English and in readily accessible American journals. The book is beautifully illustrated with 337 photographs, diagrams, and drawings, a number of which are in color.

Treatment of the Patient Past Fifty. By Ernst P. Boas, M.D. Pp. 308, with 19 illustrations. Chicago, The Year Book Publishers, Inc. $4.

In this small book of 308 pages, the author discusses at length the general philosophy of dealing with elderly patients, and constantly emphasizes the importance of consideration of the psychologic effects of the diseases, age changes, and advice to which this group is heir. There is fairly broad discussion of the management of diseases grouped in systems: cardiovascular, pulmonary, gastrointestinal, biliary, genitourinary, etc. The chief message in this book seems to be that the elderly patient requires much more constant medical attention than do younger patients, and that a great amount of thought should be given to the mental outlook. The

book must be based on personal experience, for there are fewer than four dozen references to the literature. There are but nineteen illustrations. Although the book impresses one as being far more verbose than necessary in view of the contents, nevertheless there is much sound advice in it.

An Introduction to Medical Science. By William Boyd. Ed. 2. Pp. 358, with 124 illustrations. Philadelphia, 1941, Lea & Febiger. $3.50.

This book is intended primarily for the nurse beginning her professional career. The first section of the book deals with the general principles of disease, the second with the diseased organs, and the third with some practical applications. The subject matter is written so completely and well that it is difficult to cite individual chapters for excellence. The only objection to this volume is that some of the illustrations are too diagrammatic (Figs. 42 and 76) to be clear. This book should have a wide popularity and should go through many future editions.

The Blood Bank and the Technique and Therapeutics of Transfusion. By R. A. Kilduffe and Michael DeBakey. Pp. 558, with 214 illustrations and one color plate. St. Louis, 1941, The C. V. Mosby Co. $7.50.

The opportune and timely appearance of this book is striking. Indeed, the presentation of few subjects in medicine currently would be more propitiously received than the "various considerations and more recent developments in transfusion in a readily available compendious and expository source."

The book consists of sixteen chapters including history, rationale, indications and contraindications, military aspects of transfusion, special types of transfusion, technique of blood typing and compatibility tests, the nature, causes, detection and methods for the elimination of anomalous blood-typing reactions, the "Universal Donor" and the "Universal Recipient," the blood bank and its operation and changes occurring in stored blood, preparation and preservation of fresh and processed plasma, methods and technique of transfusion, and complications of transfusion. While it is admittedly "difficult to embrace within reasonable space limits all the various phases of blood transfusion," the authors have succeeded in their "endeavor . . . to present the subject in a comprehensive manner" and "to maintain the functions of expediency and practicability." Written in an eloquent, concise, and distinctly lucid style, the authors have combined the various laboratory and clinical aspects of the subject with explicit thoroughness. Following each chapter, there is an exhaustive list of references placed in alphabetical order. That the bibliography may be "considered sufficiently extensive, varied, representative, and inclusive not only to document the text but also to serve as a reference source for those interested in the respective phases of the subject" is clearly demonstrated by the fact that the chapter on Rationale, Indications, and Contraindications contains over nine hundred references. The value of these references is further enhanced by their actual inclusion in the text.

The profuse illustrations deserve special comment. Most of these consist of line drawings executed with such refreshing vigor and distinctive simplicity as to permit unusual ease of interpretation.

In view of the fact that transfusion has recently received its greatest impetus toward a wider application and is currently undergoing intensive investigation and development, this comprehensive, authoritative, and up-to-date consideration of the subject will undoubtedly meet a ready and cordial reception by clinicians as well as laboratory technicians.

Surgical Clinics of North America. A Symposium on Military Surgery written by a number of authors, December, 1941. Volume 21, No. 6. Pp. 333, with 389 illustrations. Philadelphia, W. B. Saunders Company.

This small volume affords a review of the current military practices in the Army and Navy of the United States. Well-known authors contribute articles on the fields of their interest. The book contains much useful information on subjects of very live concern to all surgeons and can be recommended for orientation of the surgeon in our present war effort.

Thoracic Surgery. By Charles W. Lester. Ed. 1. Pp. 141. London, Oxford University Press.

This little book attempts to present in true outline form the salient information needed by physician, surgeon, and student on anatomy, physiology, anesthesia, the various disease entities of the chest, and the surgical treatment thereof. There are no illustrations. This volume should be handy for purposes of reference by one encountering this type of case frequently, but it seems too cryptic and abridged to fulfill the needs of the student, and insufficiently detailed to satisfy the thoracic surgeon. Nevertheless, it is a convenient "refresher" to have on hand for the treatment of the occasional case.